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DIAGNOSIS OF HYPERINSULINEMIA AND TYPE II DIABETES AND PROTECTION AGAINST SAME BASED ON GENES DIFFERENTIALLY EXPRESSED IN MUSCLE CELLS (15.1)

Cross-Reference to Related Applications

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Anti-Aging Applications. Mice with a disrupted growth hormone receptor/binding protein gene enjoy an increased lifespan. In U.S. Prov. Appl. 60/485,222, filed July 8, 2003 (Kopchick8) mouse genes differentially expressed in comparisons of gene expression in growth hormone receptor/binding protein gene-disrupted mouse livers and normal mouse livers were identified, as were corresponding human genes and proteins. It was suggested that the human molecules, or antagonists thereof, could be used for protection against faster-than-normal biological aging, or to achieve slower-than-normal biological aging. It was also taught that the human molecules may also be used as markers of biological aging.

In provisional application Ser. No. 60/474,606, filed June 2, 2003 (our docket Kopchick7-USA), our research group used a gene chip to study the genetic changes in the liver of C57Bl/6J mice that occur at frequent intervals of the aging process. Differential hybridization techniques were used to identify mouse genes that are differentially expressed in mice, depending upon their age. The level of gene expression of approximately 10,000 mouse genes (from the Amersham Codelink UniSet Mouse I Bioarray, product code: 300013) in the liver of mice with average ages of 35, 49, 56, 77, 118, 133, 207, 403, 558 and 725 days was determined. In essence, complementary RNA derived from mice of different ages was screened for hybridization with oligonucleotide probes each specific to a particular mouse gene, each gene in turn representative of a particular mouse gene cluster (Unigene). Mouse genes which were differentially expressed (younger vs. older), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene, were identified. Related human genes and proteins were identified by sequence comparisons to the

mouse gene or protein. In the international appl.

Kopchick7A-PCT, filed June 2, 2004, we added some additional studies of CIDE-A (see below).

In a like manner, the effect of aging on the expression of genes in mouse skeletal muscle was studied, see provisional application Ser. No. 60/566,068, filed April 29, 2004 (our docket Kopchick14-USA).

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Anti-Diabetes Applications. In U.S. Provisional Appl. Ser. No. 60/458,398 (our docket Kelder1-USA), filed March 31, 2003, members of our research group describe the identification of genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse liver. Forward- and reverse-substracted cDNA libraries were prepared, clones were isolated, and differentially expressed cDNA inserts were sequenced and compared with sequences in publicly available sequence databases. The corresponding mouse and human genes and proteins were identified.

The purpose of our research group's provisional application Ser. No. 60/460,415 (our docket: Kopchick6-USA), filed April 7, 2003, was similar, but complementary RNA, derived from RNA of mouse liver, was screened against a mouse gene chip. See also 60/506,716, filed Sept. 30, 2003 (Kopchick6.1).

Gene chip analyses have also been used to identify genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse pancreas, see U.S. Provisional Appl. 60/517,376, filed Nov. 6, 2003 (Kopchick12) and muscle, see U.S Provisional Appl. 60/547,512, filed Feb. 26, 2004 (Kopchick15).

Other differential hybridization applications. The use of differential hybridization to identify genes and proteins is also described in our research group's Ser. No. PCT/US00/12145 (Kopchick 3A-PCT), Ser. No. PCT/US00/12366 (Kopchick4A-PCT), and Ser. No. 60/400,052 (Kopchick5).

All of the foregoing applications are hereby incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to various nucleic acid molecules and proteins, and their use in (1) diagnosing hyperinsulinemia and type II diabetes, or conditions associated with their development, and (2) protecting mammals (including humans) against them.

Description of the Background Art

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Diabetes

A deficiency of insulin in the body results in diabetes mellitus, which affects about 18 million individuals in the United States. It is characterized by a high blood glucose (sugar) level and glucose spilling into the urine due to a deficiency of insulin. As more glucose concentrates in the urine, more water is excreted, resulting in extreme thirst, rapid weight loss, drowsiness, fatigue, and possibly dehydration. Because the cells of the diabetic cannot use glucose for fuel, the body uses stored protein and fat for energy, which leads to a buildup of acid (acidosis) in the blood. If this condition is prolonged, the person can fall into a diabetic coma, characterized by deep labored breathing and fruity-odored breath.

There are two types of diabetes mellitus, Type I and Type II. Type II diabetes is the predominant form found in the Western world; fewer than 8% of diabetic Americans have the type I disease.

Type I diabetes. In Type I diabetes, formerly called juvenile-onset or insulin-dependent diabetes mellitus, the pancreas cannot produce insulin. People with Type I diabetes must have daily insulin injections. But they need to avoid taking too much insulin because that can lead to insulin

shock, which begins with a mild hunger. This is quickly followed by sweating, shallow breathing, dizziness, palpitations, trembling, and mental confusion. As the blood sugar falls, the body tries to compensate by breaking down fat and protein to make more sugar. Eventually, low blood sugar leads to a decrease in the sugar supply to the brain, resulting in a loss of consciousness. Eating a sugary food can prevent insulin shock until appropriate medical measures can be taken.

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Type I diabetics are often characterized by their low or absent levels of circulating endogenous insulin, i.e., hypoinsulinemia (1). Islet cell antibodies causing damage to the pancreas are frequently present at diagnosis. Injection of exogenous insulin is required to prevent ketosis and sustain life.

Type II diabetes. Type II diabetes, formerly called adult-onset or non-insulin-dependent diabetes mellitus (NIDDM), can occur at any age. The pancreas can produce insulin, but the cells do not respond to it.

Type II diabetes is a metabolic disorder that affects approximately 17 million Americans. It is estimated that another 10 million individuals are "prone" to becoming diabetic. These vulnerable individuals can become resistant to insulin, a pancreatic hormone that signals glucose (blood sugar) uptake by fat and muscle. In order to maintain normal glucose levels, the islet cells of the pancreas produce more insulin, resulting in a condition called hyperinsulinemia. When the pancreas can no longer produce enough insulin to compensate for the insulin resistance, and thereby maintain normal glucose levels, hyperglycemia (elevated blood glucose) results, and type II diabetes is diagnosed.

Early Type II diabetics are often characterized by hyperinsulinemia and resistance to insulin. Late Type II diabetics may be normoinsulinemic or hypoinsulinemic. Type II diabetics are usually not insulin dependent or prone to ketosis under normal circumstances.

Little is known about the disease progression from the

normoinsulinemic state to the hyperinsulinemic state, and from the hyperinsulinemic state to the Type II diabetic state.

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As stated above, type II diabetes is a metabolic disorder that is characterized by insulin resistance and impaired glucose-stimulated insulin secretion (2,3,4). However, Type II diabetes and atherosclerotic disease are viewed as consequences of having the insulin resistance syndrome (IRS) for many years (5). The current theory of the pathogenesis of Type II diabetes is often referred to as the "insulin resistance/islet cell exhaustion" theory. According to this theory, a condition causing insulin resistance compels the pancreatic islet cells to hypersecrete insulin in order to maintain glucose homeostasis. However, after many years of hypersecretion, the islet cells eventually fail and the symptoms of clinical diabetes are manifested. Therefore, this theory implies that, at some point, peripheral hyperinsulinemia will be an antecedent of Type II diabetes. Peripheral hyperinsulinemia can be viewed as the difference between what is produced by the β cell minus that which is taken up by the liver. Therefore, peripheral hyperinsulinemia can be caused by increased β cell production, decreased hepatic uptake or some combination of both. It is also important to note that it is not possible to determine the origin of insulin resistance once it is established since the onset of peripheral hyperinsulinemia leads to a condition of global insulin resistance.

Multiple environmental and genetic factors are involved in the development of insulin resistance, hyperinsulinemia and type II diabetes. An important risk factor for the development of insulin resistance, hyperinsulinemia and type II diabetes is obesity, particularly visceral obesity (6,7,8). Type II diabetes exists world-wide, but in developed societies, the prevalence has risen as the average age of the population increases and the average individual becomes more obese.

Obesity and Diabetes. Obesity is a serious and growing

problem in the United States. Obesity-related health risks include high blood pressure, hardening of the arteries, cardiovascular disease, and Type II diabetes (also known as non-insulin-dependent diabetes mellitus, Type II diabetes) (9,10,11). Recent studies show that 85% of the individuals with Type II diabetes are obese (12).

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Treatment of Diabetes. For many years, treatment was insulin therapy for Type I and oral sulfonylureas and/or insulin therapy for Type II. Metformin (glucophage) was the first antidiabetic drug approved by FDA (May 1995) for the treatment of Type II diabetes since the oral sulfonylureas were introduced in 1984. Metformin promotes the use of insulin already in the blood. This May 1995 approval was followed by the September 1995 approval of another antidiabetic drug, Acarbose (precose). It slows down the digestion and absorption of complex sugars, which reduces blood sugar levels after meals.

Before 1982, insulin was purified from beef or pork pancreas. This was a problem for those diabetics allergic to animal insulin. Researchers produced a synthetic insulin called humulin. Approved by FDA in 1982, it was the first genetically engineered consumer health product manufactured for diabetics. Synthetic insulins can be produced in unlimited quantities.

Another possible treatment for diabetes includes surgically replacing the pancreas' endocrine tissues (islets of Langerhans) with healthy islet of Langerhans tissue grafts. Since 1988, 45 patients worldwide have undergone successful transplantation.

Complications. Complications of diabetes (end organ damage) include retinopathy, neuropathy, and nephropathy (traditionally designated as microvascular complications) as well as atherosclerosis (a macrovascular complication). Early stages of hyperglycemia can usually be controlled by an alteration in diet and increasing the amount of exercise, but drug treatment, including insulin, may be required. It has been shown that meticulous blood glucose control can

often slow down or halt the progression of diabetic complications if caught early enough (1). However, tight metabolic control is extremely difficult to achieve.

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Animal Models

Transgenic Mouse Models of Diabetes or Diabetes
Resistance. McGrane, et al., J. Biol. Chem. 263:11443-51
(1988) and Chen, et al., J. Biol. Chem., 269:15892-7 (1994)
describe the genetic engineering of mice to express bovine
growth hormone (bGH) or human growth hormone (hGH),
respectively. These mice exhibited an enhanced growth
phenotype. They also developed kidney lesions similar to
those seen in diabetic glomerulosclerosis, see Yang, et al.,
Lab. Invest., 68:62-70 (1993). Ogueta, et al., J.
Endocrinol., 165: 321-8 (2000) reported that transgenic mice
expressing bovine GH develop arthritic disorder and selfantibodies.

Growth hormone has many roles, ranging from regulation of protein, fat and carbohydrate metabolism to growth promotion. GH is produced in the somatrophic cells of the anterior pituitary and exerts its effects either through the GH-induced action of IGF-I, in the case of growth promotion, or by direct interaction with the GHR on target cells including liver, muscle, adipose, and kidney cells. Hyposecretion of GH during development leads to dwarfism, and hypersecretion before puberty leads to gigantism. ·adults, hypersecretion of GH results in acromegaly, a clinical condition characterized by enlarged facial bones, hands, feet, fatigue and an increase in weight. Of those individuals with acromegaly, 25% develop type II diabetes. This may be due to insulin resistance caused by the high circulating levels of GH leading to high circulating levels of insulin (Kopchick et al., Annual Rev. Nutrition 1999. 19:437-61).

A further mode of GH action may be through the transcriptional regulation of a number of genes contributing to the physiological effects of GH.

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Growth hormone genes and the proteins encoded by them can be converted into growth hormone antagonists by mutation, see Kopchick USP 5,350,836. Transgenic mice have been made that express the GH antagonists bGH-G119R or hGH G120R, and which exhibit a dwarf phenotype. Chen, et al., J. Biol. Chem., 263:15892-7 (1994); Chen, et al., Mol. Endocrinol, 5:1845-52 (1991); Chen, et al., Proc. Nat. Acad. Sci. USA 87:5061-5 (1990). These mice did not develop kidney lesions. See Yang (1993), supra.

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10 Chen, et al., Endocrinol, 136:660-7 (1995) compared the effect of streptozotocin treatment in normal nontransgenic mice, and in mice transgenic for (1) a GH receptor antagonist, the G119R mutant of bovine growth hormone or (2) the E117L-mutant of bGH. (According to Chen's ref. 24, these large GH transgenic streptozotocin-treated mice constitute an animal model for diabetes.) Glomerulosclerosis was seen in diabetic (STZ-treated) nontransgenic mice and in diabetic bGH-E117L mice, but not in diabetic bGH-G119R (GH antagonist) mice.

Two of the proteins which mediate growth hormone activity are the growth hormone receptor and the growth hormone binding protein, encoded by the same gene in mice(GHR/BP). It is possible to genetically engineer mice so that the gene encoding these proteins is disrupted ("knocked-out"; inactivated), see Zhou, et al., Proc. Nat. Acad. Sci. (USA), 94:13215-20 (1997). Zhou, et al. inactivated the GHR/BP gene by replacing the 3' portion of exon 4 (which encodes a portion of the GH binding domains) and the 5' region of intron 4 with a neomycin gene cassette. The modified gene was introduced into the target mice by homologous recombination. Like mice expressing a GH antagonist, homozygous GHR/BP-KO mice exhibit a dwarf phenotype. GHR/BP-KO mice, made diabetic by streptozotocin treatment, are protected from the development of diabetesassociated nephropathy. Bellush, et al., Endocrinol., 141:163-8 (2000).

High-Fat Diets. High-fat diets have been shown to induce both obesity and Type II diabetes in laboratory

animals (13). Surwit and colleagues demonstrated that male C57BL/6J mice are extremely sensitive to the diabetogenic effects of a high-fat diet when initiated at weaning. At six months of age, high-fat fed animals had significantly elevated fasting blood-glucose and insulin levels and also demonstrated a decrease in insulin sensitivity (14). Ahren and colleagues (15) reported evidence of insulin resistance as well as diminished glucose-stimulated insulin release, after feeding with a high-fat diet for 12 weeks. These mice also showed elevated levels of total cholesterol, triglycerides, and free fatty acids, another hallmark of Type II diabetes.

15 Anatomy and Physiology of Muscle

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Muscles may be classified by location, i.e., skeletal if attached to bone, cardiac if forming the wall of the heart, and visceral if associated with another body organ. Muscles may also be classified as voluntary or involuntary, depending on how their contractions and relaxations are controlled. Skeletal muscles are voluntary, while cardiac and visceral muscles are involuntary. It is also possible to classify muscles morphologically; skeletal and cardiac muscle cells are striated, whereas visceral muscle cells are not.

Each skeletal muscle is composed of many individual muscle cells called muscle fibers. The fibers are held together by fibrous connective-tissue membranes called fascia. The fascium which envelops the entire muscle is the epimysium, and the fascia which penetrate the muscle, separating the fibers into bundles (fasciculi) are called perimysium. Very thin fascia (endomysium) sheath each muscle fiber. Skeletal muscles are attached either directly to a bone, or indirectly through a tendon.

The individual muscle fibers (cells) comprise threadlike protein structures called myofibrils.

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There are over 600 muscles in the human body. We will have occasion later to refer to the gastrocnemius. It is a superficial muscle in the posterior compartment of the lower leg, which together with the underlying soleus forms the characteristic bulge of the calf.

Role of Muscle in Development of Type II Diabetes

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Muscle, fat and liver tissues are the major contributors to the development of insulin resistance, hyperinsulinemia, and, ultimately, type II diabetes.

Muscle cells respond to insulin by increasing glucose uptake from the bloodstream. Muscle tissue can become resistant to insulin, causing the beta cells to initially increase insulin secretion. Eventually, though, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and they fail to respond to elevated blood glucose levels. Thus, clinical type 2 diabetes results from the combination of insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance. At least three steps-those mediated by glycogen synthase, hexokinase, and GLUT4-have been reported to be defective in patients with type 2 diabetes.

Fatty acids can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase. PKC-theata has also been implicated.

See generally Petersen, et al., "Pathogenesis of Skeletal muscle insulin resistance in type 2 diabetes mellitus", in "A Symposium: Evolution of type 2 diabetes mellitus management", at Amer. J. Cardiol., 90(5A): 11G-18G, (Sept. 5, 2002).

Adverse Effects of Type II Diabetes on Muscle

"Myopathy is a general term used to describe any disease of muscles, such as the muscular dystrophies and myopathies associated with thyroid disease. It can be caused

by endocrine disorders, including diabetes, metabolic disorders, infection or inflammation of the muscle, certain drugs and mutations in genes. In diabetes, myopathy is thought to be caused by neuropathy, a complication of diabetes. General symptoms of myopathies include muscle weakness of limbs sometimes occurring during exercise although in some cases the symptoms diminish as exercise increases. Depending on the type of myopathy, one muscle group may be more affected than others." See "Joint and Muscle Problems Associated with Diabetes", www.iddtinternational.org/jointandmuscleproblems.html [Last modified June 12, 2003].

Diabetic muscle infarction can spontaneously affect patients with a long history of poorly controlled diabetes. "Most affected patients have multiple microvascular complications (neuropathy, nephropathy, and retinopathy). The clinical presentation is an acute onset of pain and swelling over days to weeks in the affected muscle groups (usually the thigh or calf), along with varying degrees of tenderness.... Therapy consists of rest and analgesia. Routine daily activities are not deleterious to the condition, but physical therapy may cause exacerbation. Spontaneous diabetic muscle infarction tends to resolve over a period of weeks to months in most cases." "Musculoskeletal Complications of Diabetes - Part 2", www.diabetic-lifestyle.com/articles/jan02 whats 1.htm [last modified Feb. 9, 2004]. See also Trujillo-Santos, et al., "Diabetes muscle infarction: an underdiagnosed complication of long-standing diabetes," Diabetes Care, 26(1):211-5 (2003).

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Identification of genes involved in hyperinsulinemia and type II diabetes, generally

Our attention recently has focused on the generation of muscle mRNA expression profiles and the identification of genes involved in the genesis of the obesity-induced hyperinsulinemia and type-II diabetes. To date, no one has attempted to study the actual progression from the normal condition to that of hyperinsulinemia or from hyperinsulinemia to Type II diabetes in an attempt to identify genes that are up-regulated or down-regulated in muscle as the disease progresses.

In previous studies aimed at identifying genes involved in diabetes-induced glomerulosclerosis, differential display and traditional subtractive hybridization techniques were used (16-20). While effective for the identification of a few genes (e.g. hmunc13, PED/PEA-15, lactate dehydrogenase, amiloride sensitive sodium channel, ubiquitin-like protein, mdr 1, and a-amyloid protein precursor as well as a few novel genes), these techniques can be quite labor intensive. The PCR-based method of subtractive hybridization requires less starting material, and allows the simultaneous isolation of all differentially expressed cDNAs into two groups (up-regulated and down-regulated).

However, the PCR-based method of subtractive hybridization is also quite labor-intensive, produced large numbers of false positive candidates and ultimately resulted in the identification of a relatively limited number of differentially expressed genes. (see Kelder1-USA application).

In order to expand the number of genes that can be analyzed simultaneously, several groups have begun to utilize DNA microarray analysis to measure differences in gene expression between normal and diseased states.

However, these experiments have been limited in regards to the number of experimental conditions analyzed. DNA microarray analysis has been performed on normal, obese and diabetic mice (21). Also, the obesity and diabetes in the

mouse models examined were caused by a specific endogenous genetic mutation (22). The differentially expressed genes in the above models may be very different from genes differentially expressed due to diet-induced obesity and Type-II diabetes.

The use of differential expression and related techniques to identify genes useful in the treatment of diabetes has been reviewed by Perfetti, et al., Diabetes Technol. & Therapeut., 5(3): 421-3 (2003). Bernal-Mizrachi, et al., Diabetes Metab. Res. Rev. 19: 32-42 (2003).

Other papers of interest include:

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Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", Kidney Int, 59:1363-73 (2001);

Song, et al., "Cloning of a novel gene in the human kidney homologous to rat muncl3S: its potential role in diabetic nephropathy", Kidney Int., 53:1689-95 (1998);

Page, et al., "Isolation of diabetes-associated kidney genes using differential display", Biochem. Biophys. Res. Comm., 232:49-53 (1997).

Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," Kidney Int. 53:926-31 (1998).

Condorelli, EMBO J., 17:3858-66 (1998).

Diabetes-Specific Differential Expression in Muscle

Sreekumar, et al., "Gene expression profile in skeletal msucle of type 2 diabetes and the effect of insulin treatment," Diabetes 51: 1913 (June 2002) surveyed 6,451 genesw, and identified 85 genes for which there was an alteration in skeletal muscle transcription in diabetic patients after withdrawal of insulin treatment. Subsequent insulin treatment resulted in further changes in transcription of 74 of the 85 genes (15 increased, 59 decreased), and also resulted in alteration of 29 additional gene transcripts.

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Mootha, et al., "PCG-10 responsive genes involved in oxidative phosphorylation are coordinatively downregulated in human diabetes," Nature Genetics 34(3); 267 (July 2003), used DNA microarrays to detect changes in the expression of sets of related genes, rather than of individual genes. They classified over 22,000 genes into 149 data sets; some of these data sets overlapped. They looked for a statistical correlation between the overall rank order of the genes in differential expression, and the groups to which the genes belonged. Expression was compared pairwise among three groups: males with normal glucose tolerance; males with impaired glucose tolerance; and males with type 2 diabetes. The set with the highest enrichment score (the one whose members ranked highly most often relative to chance expectation) was an internally curated set of 106 genes involved in oxidative phosphorylation. While the average decrease for the individual genes was modest (~20%), it was also consistent, being observed in 89% (94/106) of the genes in question. This paper is reviewed by Toye and Gauquier, "Genetics and functional genomics of type 2 diabetes mellitus", Genome Biology, 4: 241 (2003).

Patti, et al., "Coordinated reduction of genes of oxidative metabolism in humans with insulin resistance and diabetes: Potential role of PGC1 and NRF1", Proc. Nat. Acad. SCi. (USA), 100(14): 8466 (July 8, 2003) used microarrays to analyze skeletal muscle expression of genes in nondiabetic insulin-resistant subjects at high risk for diabetes (based on family hisotry of diabetes and Mexican-American ethnicity) and diabetic Mexican-American subjects. Of 7,129 sequences represented on the microarray, 187 were differentially expressed between control and diabetic However, no single gene remained significantly differentially expressed after controlling for multiple comparison false discovery by using the Benjamini-Hochberg method, see Benjamini, et al., J. R. Stat. Soc. Sert. B. 57:289-300 (1995); Dudait, et al., Stat. Sin. 12: 111-139 Consequently, Patti et al. sought to identify

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groups of related genes with similar patterns of differential expression using MAPP FINDER and ONTOEXPRESS. According to MAPP FINDER, the top-ranked cellular component terms were mitochondrion, mitochondrial membrane, mitochondrial inner membrane, and ribosome, and the top-ranked process term was ATP biosynthesis. According to ONTOEXPRESS, the over-represented groups were energy generation, protein biosynthesis/ribosomal proteins, RNA binding, ribosomal structural protein, and ATP synthase complex.

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Huang, Xudong, "Identification of abnormally expressed genes in skeletal muscle contributing to insulin resistance and type 2 diabetes", Thesis, document id: 9576 Lunds University 2002, reported differential expression of the mitochondrially-encoded ND1 gene in human diabetic patients and of the nuclear-encoded cathepsin L gene in mice.

Standaert, et al., ":Skeletal muscle insulin resistance in obesity-associated type 2 diabetes in monkeys is linked to a defect in insulin activation of protein kinase C-zeta/lambda/iota Diabetes 51: 2936 (Oct. 2002). the authors concluded that defective activation of atypical PKCs played an important role in the patehogenesis of peripheral insulin resistance in both obese prediabetic and diabetic monkeys. They attributed this linkage to the apparent requirement for aPKCs during insulin-stimulated glucose transport.

Srommer, et al., Am. J. Physiol., "Skeletal muscle insulin resistance after trauma: insulin signaling and glucose transport", 275(2 Pt. 1): E3518(Aug. 1998) concluded that insulin resistance in skeletal muscle after surgical trauma is associated with reduced glucose transport but not with impaired glucose signaling to PI 3-kinase or its downstream target, Akt.

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Gene Chip-Based Identification of genes involved in aging of skeletal muscle

Several groups have used DNA microarrays to measure differences in gene expression caused by the aging process. However, these experiments are extremely limited in regards to the number of aging time points or experimental conditions.

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Weindruch, et al., "Microarray profiling of gene expression in aging and its alteration by caloric restriction in mice" in Symposium: Calorie Restriction: effects on Body Composition, Insulin Signaling and Aging 918S-923S (2001) (21) compared expression in gastrocnemius muscle from 5- and 30-month old C57BL/6 mice, with and without caloric restriction. In this analysis, the expression of 113 genes was found to be changed by at least two-fold in 5-month old mice compared to 30-month old mice. Caloric restriction of comparable mice caused a reversal of the altered gene expression of 33 genes.

Of the 6347 genes surveyed in the oligonucleotide microarray, only 58 (0.9%) displayed a greater than 2 fold increase in gene expression as a function of aging, whereas 55(0.9%) displayed a greater than 2 fold decrease.

Of the genes positively correlated with aging, 16% could be assigned to stress responses. The largest differential expression between young and aged animals (3.8 fold) was the mitochondrial sarcomeric creatine kinase.

Of the genes negatively correlated with aging, 13% were involved in energy metabolism. A noteworthy number were genes encoding biosynthetic enzymes (cytochrome P450 IIC12, squaelene synthase, stearoyl-CoA desaturase, EF-1-gamma. Another down regulator was a CpG binding protein, MeCP2.

Weindruch further reported that age-related changes in gene expression profile were "remarkably attenuated" by caloric restriction.

What appears to be the same experiment is discussed in Lee, et al., "Gene expression profile of aging and its retardation by caloric restriction," Science, 285: 1390 (Aug. 27, 1999). This papers lists the individual genes which

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were differentially expressed by more than 2-fold, and classifies them as energy metabolism, neuronal factors, protein metabolism, stress response, biosynthesis, calcium metabolism or DNA repair genes.

Welle, et al., "Skeletal muscle gene expression profiles in 20-29 year old and 65-71 year old women," Exper. Gerontol., 39: 369-77 (2004) and available electronically as doi:10.1016/j.exger.2003.11.011 studied gene expression and physical condition in seven young and eight older women. With respect to physical condition, the measured or calculated parameters were total body mass, lean body mass, left leg lean mass (by biopsy), maximum isometric left knee extension force, left knee extension force/left keg lean mass, Peak VO2/lean body mass, and Peak VO2/left leg lean mass.

There were 1178 "probe sets" (representing 1053 different Unique clusters) for which differential expression was detected; 550 for which expression was higher in older women, and 628 the inverse effect. The differences ranged from 1.2 to 4 fold; most (78A%) were less than 1.5 fold. The complete list of differentially expressed genes is given in the Rochester Muscle database website, www.urmc.rochester.edu/smd/crc/swindex (".html" omitted, in accordance with USPTO requirements, so that the publication of this application will not create an active hyperlink).

The gene most highly overexpressed in older muscle was p21 (cyclin-dependent kinase inhibitor 1A) (4.01 fold). This one of several genes (see Welle Table 2) which are potentially related to DNA damage and repair. Welle also thought it noteworthy how many of the differentially expressed genes were ones that encode proteins which bind to pre-mRNAs or mRNAs (see Welle Table 3).

Other Differential/Subtractive Hybridization Studies of Interest .

Zhang, et al., Kidney International, 56:549-558 (1999) identified genes up-regulated in 5/6 nephrectomized

(subtotal renal ablation) mouse kidney by a PCR-based subtraction method. Ten known and nine novel genes were identified. The ultimate goal was to identify genes involved in glomerular hyperfiltration and hypertrophy. Melia, et al., Endocrinol., 139:688-95 (1998) applied subtractive hybridization methods for the identification of androgen-regulated genes in mouse kidney. The treatment mice were dosed with dihydrotestosterone, an androgen. Kidney androgen-regulated protein gene was used as a positive control, as it is known to be up-regulated by DHT.

See also Holland, et al., Abstract 607, "Identification of Genes Possibly Involved in Nephropathy of Bovine Growth Hormone Transgenic Mice" (Endocrine Society Meeting, June 22, 2000) and Coschigano, et al., Abstract 333, "Identification of Genes Potentially Involved in Kidney Protection During Diabetes" (Endocrine Society Meeting, June 22, 2000).

The following differential hybridization articles may also be of interest: Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", Kidney Int, 59:1363-73 (2001); Song, et al., "Cloning of a novel gene in the human kidney homologous to rat muncl3S: its potential role in diabetic nephropathy", Kidney Int., 53:1689-95 (1998); Page, et al., "Isolation of diabetes-associated kidney genes using differential display", Biochem. Biophys. Res. Comm., 232:49-53 (1997); Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," Kidney Int. 53:926-31 (1998); Condorelli, EMBO J., 17:3858-66 (1998).

Apoptosis and CIDE-A

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Apoptosis is a form of programmed cell death that occurs in an active and controlled manner to eliminate unwanted cells. Apoptotic cells undergo an orchestrated cascade of morphological changes such as membrane blebbing,

nuclear shrinkage, chromatin condensation, and formation of apoptotic bodies which then undergo phagocytosis by neighboring cells. One of the hallmarks of cellular apoptosis is the cleavage of chromosomal DNA into discrete oligonucleosomal size fragments. This orderly removal of unwanted cells minimizes the release of cellular components that may affect neighboring tissue. In contrast, membrane rupture and release of cellular components during necrosis often leads to tissue inflammation.

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The process of apoptosis is highly conserved and involves the activation of the caspase cascade. Cohen, GM. (1997) Caspases: the executioners of apoptosis. Biochem. J. 326:1-16; Budihardjo, I., Oliver, H., Lutter, M., Luo, X., Wang, X. (1999) Biochemical pathways of caspase activation during apoptosis. Annnu. Rev. Cell. Dev. Biol.15:269-290; Jacobson, M.D., Weil, M., Raff, M.C. (1997) Programmed cell death in animal development. Cell 88:347-354. Caspases are a family of serine proteases that are synthesized as inactive proenzymes. Their activation by apoptotic signals such as CD95 (Fas) death receptor activation or tumor necrosis factor results in the cleavage of specific target proteins and execution of the apoptotic program. Apoptosis may occur by either an extrinsic pathway involving the activation of cell surface death receptors (DR) or by an intrinsic mitochondrial pathway. Yoon, J-H. Gores G.J. (2002) Death receptor-mediated apoptosis and the liver. J. Hepatology 37:400-410.

These pathways are not mutually exclusive and some cell types require the activation of both pathways for maximal apoptotic signaling. In type-I cells, death receptor activation leads to the recruitment and activation of caspases-8/10 and the rapid cleavage and activation of caspase-3 in a mitochondrial-independent manner. Hepatocytes are members of the Type-II cells in which mitochondria are essential for DR-mediated apoptosis Scaffidi, C., Fulda, S., Srinivasan, A., Friesen, C., Li, F., Tomaselli, K.J., Debatin, K.M., Krammer, P.H., Peter, M.E. (1998) Two CD95 (APO-1/Fas) signaling pathways. EMBO J. 17:1675-1687. In this pathway, the pro-apoptotic protein

Bid is truncated by activated caspases-8/10 and translocates to the mitochondria. Luo, X., Budihardjo, I., Zou, H., Slaughter, C., Wang, X. (1998) Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. Cell 94:481-490; Li, H., Zhu, H., Xu, C.J., Yuan, J. (1998) Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis. Cell 94:491-501. This translocation leads to mitochondrial cytochrome c release and eventual activation of caspases-3 and 7 via cleavage by activated caspase-9.

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One of the substrates for activated caspase-3 is the DNA fragmentation factor (DFF). DFF is composed of a 45 kDa regulatory subunit (DFF45) and a 40 kDA catalytic subunit (DFF40). Liu, X., Zou, H., Slaughter, C., Wang, (1997) DFF, a heterodimeric protein that х. downstream of caspase-3 to trigger DNA fragmentation during apoptosis. Cell 89:175-184. DFF45 cleavage by activated caspase-3 results in its dissociation from DFF40 and allows the caspase-activated DNAse (CAD) activity of DFF40 to cleave chromosomal DNA into oligonucleosomal size fragments. Liu, X., Li, P., Widlak, P., Zou, H., Luo, X., Garrard, W.T., Wang, X. (1998) The 40-kDa subunit of DNA fragmentation factor induces DNA fragmentation and chromatin condensation during apoptosis. Proc. Natl. Acad. Sci. USA. 95:8461-8466; Halenbeck, R., MacDonald, H., Roulston, A., Chen, T.T., Conroy, L., Williams, L.T. (1998) CPAN, a human nuclease regulated by the caspase-sensitive inhibitor DFF45. Curr Biol. 8:537-540; Nagata, S. (2000) Apoptotic DNA fragmentation. Exp. Cell Res. 256:12-8.

Recently, a novel family of cell-death-inducing DFF45-like effectors (CIDEs) have been identified that includes CIDE-A, CIDE-B and CIDE-3/FSP2. Inohara, N., Koseki, T., Chen, S., Wu, X., Nunez, G. (1998) CIDE, a novel family of cell death activators with homology to the 45 kDa subunit of the DNA fragmentation factor. EMBO J. 17:2526-2533; Danesch, U., Hoeck, W., Ringold, G.M. (1992) Cloning and transcriptional regulation of a novel adipocytespecific gene, FSP27. CAAT-enhancer-binding protein (C/EBP)

and C/EBP-like proteins interact with sequences required for differentiation-dependent expression. J. Biol. Chem. 267:7185-7193; Liang, L., Zhao, M., Xu, Z., Yokoyama, K.K., Li, T. (2003) Molecular cloning and characterization of CIDE-3, a novel member of the cell-death-inducing DNA-fragmentation-factor (DFF45)-like effector family. Biochem. J. 370:195-203.

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The CIDEs contain an N-terminal domain that shares homology with the N-terminal region of DFF45 and may represent a regulatory region via protein interaction. See Inohara, supra; Lugovskoy, A.A., Zhou, P., Chou, J.J., McCarty, J.S., Li, P., Wagner, G. (1999) Solution structure of the CIDE-N domain of CIDE-B and a model for CIDE-N/CIDE-N interactions in the DNA fragmentation pathway of apoptosis. Cell 9:747-755. The family members also share a C-terminal domain that is necessary and sufficient for inducing cell death and DNA fragmentation; see Inohara The overexpression of CIDE-A induces cell death that can be inhibited by DFF45. However, CIDE-A-induced apoptosis is not inhibited by caspase-8 inhibitors thereby suggesting the presence of additional, caspase-independent, pathway(s) for the induction of apoptosis, see Inohara supra. Previous reports have indicated that human and mouse CIDE-A are expressed in several tissues such as brown adipose tissue (BAT) and heart and are localized to the mitochondria, Zhou, Z., Yon Toh, S., Chen, Z., Guo, K., Ng, C.P., Ponniah, S., Lin, S.C., Hong, W., Li, P. (2003) Cidea-deficient mice have lean phenotype and are resistant to obesity. Nat. Genet. 35:49-56. . In addition to the ability to induce apoptosis, CIDE-A can interact and inhibit 'UCP1 in BAT and may therefore play a role in regulating energy balance, see Zhou supra.

Previous reports have indicated that CIDE-A is not expressed in either adult human or mouse liver tissue, see Inohara supra, Zhou supra.

The human protein cell death activator CIDE-A is of particular interest because of its highly dramatic change in liver expression with age, first demonstrated in our

Kopchick7 application, supra. CIDE-A expression is elevated in older normal mice. CIDE-A expression was studied for normal C57BI/6J mouse ages 35, 49, 77, 133, 207, 403 and 558 days. Expression is low at the first five data points, then rises sharply at 403 days, and again at 558 days.

CIDE-A was therefore classified as an "unfavorable protein", i.e., it was taught that an antagonist to CIDE-A could retard biological aging.

In Kopchick7A-PCT we reported that CIDE-A is also prematurely expressed in hyperinsulinemic and type-II diabetic mouse liver tissue. CIDE-A expression also correlates with liver steatosis in diet-induced obesity, hyperinsulinemia and type-II diabetes. These observations suggest an additional pathway of apoptotic cell death in Non-Alcoholic Fatty Liver Disease (NAFLD) and that CIDE-A may play a role in this serious disease and potentially in liver dysfunction associated with type-II diabetes.

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SUMMARY OF THE INVENTION

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Differential hybridization techniques have been used to identify mouse genes that are differentially expressed in the muscle (gastrocnemius) of mice, depending upon their development of hyperinsulinemia or type II diabetes.

In essence, complementary RNA derived from normal mice, or mouse models of hyperinsulinemia or type II diabetes, was screened for hybridization with oligonucleotide probes each specific to a particular mouse database DNA, the latter being identified, by database accession number, by the gene manufacturer. Each database DNA in turn was also identified by the gene chip manufacturer as representative of a particular mouse gene cluster (Uniqene).

In most cases, this database DNA sequence is a full length genomic DNA or cDNA sequence, and is therefore either identical to, or otherwise encodes the same protein as does, a natural full-length genomic DNA protein coding sequence. Those which don't present at least a partial sequence of a natural gene or its cDNA equivalent.

For the sake of simplicity, all of these mouse database DNA sequences, whether full-length or partial, and whether cDNA or genomic DNA, are referred to herein as "mouse genes". When only the genomic sequence is intended, we will refer specifically to "genomic DNA" or "gDNA".

The sequences in the protein databases are determined either by directly sequencing the protein or, more commonly, by sequencing a DNA, and then determining the translated amino acid sequence in accordance with the Genetic Code. All of the mouse sequences in the mouse polypeptide database are referred to herein as "mouse proteins" regardless of whether they are in fact full length sequences.

Mouse genes which were differentially expressed (normal vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or normal vs. diabetic), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene) were identified.

Since the progression is from normal to hyperinsulinemic, and thence from hyperinsulinemic to type II diabetic, one may define mammalian subjects as being more favored or less favored, with normal subjects being more favored than hyperinsulinemic subjects, and hyperinsulinemic subjects being more favored than type II diabetic subjects. The subjects' state may then be correlated with their gene expression activity.

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The terms "normal" and "control" are used interchangeably in this specification, unless expressly stated otherwise. The control or normal subject is a mouse which is normal vis-a-vis fasting insulin and fasting glucose levels. The term "normal", as used herein, means normal relative to those parameters, and does not necessitate that the mouse be normal in every respect.

A mouse gene is said to have exhibited a favorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is higher than that in mice which are in a less favored state. A mouse gene is said to have exhibited an unfavorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is lower than that in mice which are in a less favored state.

When we observe the mice at several different ages, it is possible for their expression behavior to vary from time point to time point. For a given comparison of subjects, e.g., normal vs. hyperinsulinemic, we classify the mouse gene as favorable or unfavorable on the basis of the direction of the largest expression change, and it is the magnitude of this largest expression change, expressed as a ratio of greater to lesser, which is set forth in the Master Table 1 data for that mouse gene. Thus, if at 2 weeks, there was a 3-fold favorable behavior, and at 8 weeks, there was a 4-fold unfavorable behavior, and at all other observed time points, the behavior was weaker than 3-fold, the mouse gene would be classified as an unfavorable gene with respect to the subject comparison in question.

It will be appreciated that it may be that if the mouse gene were observed at an age other than one of the ages noted in the Examples, we would have observed a still stronger differential expression behavior. Nonetheless, we must classify the mouse genes on the basis of the behavior which we actually observed, not the behavior which might have been observed at some other age.

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We are particularly interested in mouse genes which exhibit strongly favorable or unfavorable differential expression behaviors. A behavior is considered strong if the ratio of the higher level to the lower level is at least two-fold.

However, a mouse gene may still be identified as favorable or unfavorable even if none of its observed behaviors are strong as defined above. In general, we consider the consistency of its behaviors (that is, are all or most of the differential expression behaviors at different ages in the same direction, e.g., hyperinsulinemic higher than control), the magnitude of the behaviors (higher the better), and the expression behavior of structurally or functionally related mouse genes (a mouse gene is more likely to be identified as favorable on the basis of a weakly favorable behavior if it is related to other mouse genes which exhibited favorable, especially strongly favorable, behavior). If we considered a mouse gene with only weak differential expression behavior to be worthy of consideration on the basis of these criteria, then we listed it in Master Table 1 in the appropriate subtable.

Preferably, the differential behavior observed is both strong and consistent. Preferably, if related mouse genes were tested, they exhibit the same direction of differential expression behavior.

A mouse gene which was more strongly expressed in hyperinsulinemic tissue than in either normal or type II diabetic tissue (i.e., C<HI, HI>D) will be deemed both "unfavorable", by virtue of the control:hyperinsulinemic comparison, and "favorable", by virtue of the

hyperinsulinemic:diabetic comparison. This is one of several possible "mixed" expression patterns.

Thus, we can subdivide the "favorables" into wholly and partially favorables. Likewise, we can subdivide the unfavorables into wholly and partially unfavorables. The genes/proteins with "mixed" expression patterns are, by definition, both partially favorable and partially unfavorable. In general, use of the wholly favorable or wholly unfavorable genes/proteins is preferred to use of the partially favorable or partially unfavorable ones.

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It is evident from the foregoing that mixed genes/proteins are those exhibiting a combination of favorable and unfavorable behavior. A mixed gene/protein can be used as would a favorable gene/protein if its favorable behavior outweighs the unfavorable. It can be used as would an unfavorable gene/protein if its unfavorable behavior outweighs the favorable. Preferably, they are used in conjunction with other agents that affect their balance of favorable and unfavorable behavior. Use of mixed genes/proteins is, in general, less desirable than use of purely favorable or purely unfavorable genes/proteins, but it is not excluded.

It should be noted that a mouse gene is classified on the basis of the strongest C-HI behavior among the ages tested, the strongest HI-D behavior among the ages tested, and the strongest C-D behavior among the ages tested. If at least one of these three behaviors is significantly favorable, and none of the others of these three behaviors is significantly unfavorable, the mouse gene will be classified as wholly favorable and listed in subtable 1A of Master Table 1. However, that does not mean that it may not have exhibited a weaker but unfavorable expression behavior at some tested age.

The "favorable", "unfavorable" and "mixed" mouse proteins of the present invention include the mouse database proteins listed in the Master Table in the same row as a particular "favorable", "unfavorable" or "mixed" mouse gene, respectively. These proteins may be the exact translation product of the identified mouse gene (database DNA).

However, if they were sequenced directly, they could be shorter or longer than that translation product. They could also differ in sequence from the exact translation product as a result of post-translational modifications.

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The mouse proteins of interest also include mouse proteins which, while not listed in the table, correspond to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) such mouse proteins or genes, and mouse proteins which are at least substantially identical or conservatively identical to the listed mouse proteins.

Related human genes (database DNAs) and proteins were identified by searching a database comprising human DNAs or proteins for sequences corresponding to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) the mouse gene or protein. More than one human protein may be identified as corresponding to a particular mouse chip probe and to a particular mouse gene.

Note that the terms "human genes" and "human proteins" are used in a manner analogous to that already discussed in the case of "mouse genes" and "mouse proteins".

As used herein, the term "corresponding" does not mean identical, but rather implies the existence of a statistically significant sequence similarity, such as one sufficient to qualify the human protein or gene as a homologus protein or DNA as defined below. The greater the degree of relationship as thus defined (i.e., by the statistical significance of each alignment used to connect the mouse cDNA to the human protein or gene, measured by an E value), the more close the correspondence. The connection may be direct (mouse gene to human protein) or indirect (e.g., mouse gene to human gene, human gene to human protein). By "mouse gene", we mean the mouse gene from which the gene chip DNA in question was derived.

In general, the human genes/proteins which most closely correspond, directly or indirectly, to the mouse genes are preferred, such as the one(s) with the highest, top two

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highest, top three highest, top four highest, top five highest, and top ten highest E values for the final alignment in the connection process. The human genes/proteins deemed to correspond to our mouse genes are identified in the Master Tables.

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Note that it is possible to identify homologous fulllength human genes and proteins, if they are present in the database, even if the query mouse DNA or protein sequence is not a full-length sequence.

If there is no homologous full-length human gene or protein in the database, but there is a partial one, the latter may nonetheless be useful. For example, a partial protein may still have biological activity, and a molecule which binds the partial protein may also bind the full-length protein so as to antagonize a biological activity of the full-length protein. Likewise, a partial human gene may encode a partial protein which has biological activity, or the gene may be useful in the design of a hybridization probe or in the design of a therapeutic antisense DNA.

The partial genes and protein sequences may of course also be used in the design of probes intended to identify the full length gene or protein sequence.

For the sake of convenience, we refer to a human protein as favorable if (1) it is listed in Master Table 1 as corresponding to a favorable mouse gene, or (2) it is at least substantially identical or conservatively identical to a listed protein per (1), or (3) it is a member of a human protein class listed in Master Table 2 (if provided) as corresponding to a favorable mouse gene. We define a human protein as unfavorable in an analogous manner. We may further identify a human protein as being wholly favorable (see mouse genes of subtable 1A, wholly unfavorable (see mouse genes of subtable 1B), or mixed, i.e., both partially favorable and partially unfavorable (see mouse genes of subtable 1C).

Likewise, a human gene which encodes a particular human protein may be classified in the same way as the human protein which it encodes.

However, it should be noted that this classification is not based on the direct study of the expression of the human gene/protein. of course, the human genes/proteins of ultimate interest will be the ones whose change in level of expression is, in fact, correlated, directly or inversely, with the change of state (normal, hyperinsulinemic, diabetic) of the subject.

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After identifying related human genes and proteins, one may formulate agents useful in screening humans at risk for progression toward hyperinsulinemia or toward type II diabetes, or protecting humans at risk thereof from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

Agents which bind the "favorable" and "unfavorable" nucleic acids (e.g., the agent is a substantially complementary nucleic acid hybridization probe), or the corresponding proteins (e.g., an antibody vs. the protein) may be used to evaluate whether a human subject is at increased or decreased risk for progression toward type II diabetes. A subject with one or more elevated "unfavorable" and/or one or more depressed "favorable" genes/proteins is at increased risk, and one with one or more elevated "favorable" and/or one or more depressed "unfavorable" genes/proteins is at decreased risk. One may further take into account whether the subject is normoinsulinemic or hyperinsulinemic at the time of the assay. If the subject is non-diabetic and normoinsulinemic, we are especially interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in hyperinsulinemic vs. normal muscle. If the subject is already hyperinsulinemic, yet non-diabetic, we are especially interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in type II diabetic vs. hyperinsulinemic muscle.

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The assay may be used as a preliminary screening assay to select subjects for further analysis, or as a formal diagnostic assay.

The identification of the related genes and proteins may also be useful in protecting humans against these disorders.

Thus, Applicants contemplate:

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- (1) use of the "favorable" mouse DNAs (or fragments thereof) of the Master Tables (below) to isolate or identify related human DNAs;
- (2) use of human DNAs, related to favorable mouse DNAs, to express the corresponding human proteins;
- (3) use of the corresponding human proteins (and mouse proteins, if biologically active in humans), to protect against the disorder(s);
- (4) use of the corresponding mouse or human proteins, or nucleic acid probes derived from the mouse or human genes, in diagnostic agents, in assays to measure progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage; and
- (5) use of the corresponding human or mouse genes therapeutically in gene therapy, to protect against the disorder(s).

Moreover Applicants contemplate:

- (1) use of the "unfavorable" mouse DNAs (or fragments thereof) of the Master Tables to isolate or identify related human DNAs;
- (2) use of the complement to the "unfavorable" mouse DNAs or related human DNAs, as antisense molecules to inhibit expression of the related human DNAs;
- (3) use of the mouse or human DNAs to express the corresponding mouse or human proteins;
- (4) use of the corresponding mouse or human proteins, in diagnostic agents, to measure progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage;

(5) use of the corresponding mouse or human proteins in assays to determine whether a substance binds to (and hence may neutralize) the protein; and

(6) use of the neutralizing substance to protect against the disorder(s).

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Thus, DNAs of interest include those which specifically hybridize to the aforementioned mouse or human genes, and are thus of interest as hybridization assay reagents or for antisense therapy. They also include synthetic DNA sequences which encode the same polypeptide as is encoded by the database DNA, and thus are useful for producing the polypeptide in cell culture or in situ (i.e., gene therapy). Moreover, they include DNA sequences which encode polypeptides which are substantially structurally identical or conservatively identical in amino acid sequence to the mouse and human proteins identified in the Master Table 1, subtables 1A or 1C. Finally, they include DNA sequences which encode peptide (including antibody) antagonists of the proteins of Master Table 1, subtables 1B or 1C.

The related human DNAs may be identified by comparing the mouse sequence (or its AA translation product) to known human DNAs (and their AA translation products).

Related human DNAs also may be identified by screening human cDNA or genomic DNA libraries using the mouse gene of the Master Table, or a fragment thereof, as a probe.

If the mouse gene of Master Table 1 is not full-length, and there is no closely corresponding full-length mouse gene in the sequence databank, then the mouse DNA may first be used as a hybridization probe to screen a mouse cDNA library to isolate the corresponding full-length sequence.

Alternatively, the mouse DNA may be used as a probe to screen a mouse genomic DNA library.

Our animal models of hyperinsulinemia and diabetes are also obese. It is possible that the genes found to be favorable act indirectly by inhibiting obesity. Likewise, it is possible that the genes found to be unfavorable act indirectly by accentuating obesity. Consequently, it is

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within the compass of the present invention to use the favorable genes and proteins, or to use antagonists of the unfavorable genes and proteins, to protect against obesity, as well as against sequelae of obesity such as hyperinsulinemia and diabetes.

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Since type II diabetes is an age-related disease, the agents of the present invention may be used in conunction with known anti-aging or anti-age-related disease agents. It is of particular interest to use the agents of the present invention in conjunction with an agent disclosed in one of the related applications cited above, in particular, an antagonist to CIDE-A, the latter having been taught in Kopchick7 and Kopchick7A-PCT.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Body weight gain [Fig. 1a], fasting glucose [Fig. 1b] and fasting insulin [Fig. 1c] levels of mice on the HF or Std diets.

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Figure 2. Expression levels of Actin, alpha, cardiac (Actc1, NM_009608) using RNA isolated from gastrocnemius muscle of individual diabetic HF mice and corresponding Std mice at different time points.

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Figure 3. Data shown are expression levels for additional actin-related and actin-binding genes exhibiting a consistent decrease in expression in the HF mice in comparison to Std mice at all four time points (Fig. 3(a)) or at three of the four time points (Fig. 3(b)).

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS OF THE INVENTION

Full-Length vs. Partial Length Genes/Proteins

A "full length" gene is here defined as (1) a naturally occurring DNA sequence which begins with an initiation codon (almost always the Met codon, ATG), and ends with a stop codon in phase with said initiation codon (when introns, if any, are ignored), and thereby encodes a naturally occurring polypeptide with biological activity, or a naturally occurring precursor thereof, or (2) a synthetic DNA sequence which encodes the same polypeptide as that which is encoded by (1). The gene may, but need not, include introns.

A "full-length" protein is here defined as a naturally occurring protein encoded by a full-length gene, or a protein derived naturally by post-translational modification of such a protein. Thus, it includes mature proteins, proproteins, preproteins and preproproteins. It also includes substitution and extension mutants of such naturally occurring proteins.

Subjects

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A mouse is considered to be a diabetic subject if, regardless of its fasting plasma insulin level, it has a fasting plasma glucose level of at least 190 mg/dL. A mouse is considered to be a hyperinsulinemic subject if its fasting plasma insulin level is at least 0.67 ng/mL and it does not qualify as a diabetic subject. A mouse is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

A mouse is considered "obese" if its weight is at least 15% in excess of the mean weight for mice of its age and sex. A mouse which does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

A human is considered a diabetic subject if, regardless of his or her fasting plasma insulin level, the fasting plasma glucose level is at least 126 mg/dL. A human is considered a hyperinsulinemic subject if the fasting plasma insulin level is more than 26 micro International Units/mL (it is believed that this is equivalent to 1.08 ng/mL), and does not qualify as a diabetic subject. A human is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

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A human is considered "obese" if the body mass index (BMI) (weight divided by height squared) is at least 30 kg/m². A human who does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

A human is considered overweight if the BMI is at least $25~kg/m^2$. Thus, we define overweight to include obese individuals, consistent with the recommendations of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). A human who does not satisfy this standard may be characterized as "non-overweight."

According to the Report of the Expert Committe on the Diagnosis and Classification of Diabetes Mellitus, Diabetes Care 20: 1183-97 (1997), the following are risk factors for diabetes type II:

older (e.g., at least 45; see below)

excessive weight (see below)

first-degree relative with diabetes mellitus

member of high risk ethnic group (black, Hispanic, Native American, Asian)

history of gestational diabetes mellitus or delivering a baby weighing more than 9 pounds (4.032 kg)

hypertensive (>140/90 mm Hg)

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HDL cholesterol level >35 mg/dL (0.90 mmol/L)

triglyceride level >=250 mg/dL (2.83 mmol/L)

Hence, in a preferred embodiment, the diagnostic and protective methods of the present invention are applied to human subjects exhibiting one or more of the aforementioned risk factors. Likewise, in a preferred embodiment, they are applied to human subjects who, while not diabetic, exhibit impaired glucose homeostasis (110 to <126 mg/dL).

The risk of diabetes increases with age. Hence, in successive preferred embodiments, the age of the subjects is at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, and at least 75.

With regard to excessive weight, NLDDK says that "The relative risk of diabetes increases by approximately 25 percent for each additional unit of BMI over 22." Hence, in successive preferred embodiments, the BMIs of the human subjects is at least 23, at least 24, at least 25 (i.e., overweight by our criterion), at least 26, at least 27, at least 28, at least 29, at least 30 (i.e., obese), at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at least 38, at least 39, at least 40, or over 40.

Age-Related Diseases

Age-related (senescent) diseases include certain cancers, atherosclerosis, diabetes (type 2), osteoporosis, hypertension, depression, Alzheimer's, Parkinson's, glaucoma, certain immune system defects, kidney failure, and liver steatosis. In general, they are diseases for which the relative risk (comparing a subpopulation over age 55 to a suitably matched population under age 55) is at least 1.1.

Preferably, the agents of the present invention protect against one or more age-related diseases for at least a subpopulation of mature (post-puberty) adult subjects.

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Direct and Indirect Utility of Identified Nucleic Acid Sequences and Related Molecules

The mouse or human genes (or fragments thereof) may be used directly. For diagnostic or screening purposes, they (or specific binding fragments thereof) may be labeled and used as hybridization probes. For therapeutic purposes, they (or specific binding fragments thereof) may be used as antisense reagents to inhibit the expression of the corresponding gene, or of a sufficiently homologous gene of another species.

If the database DNA appears to be a full-length cDNA or gDNA, that is, it encodes an entire, functional, naturally occurring protein, then it may be used in the expression of that protein. Likewise, if the corresponding human gene is known in full-length, it may be used to express the human protein. Such expression may be in cell culture, with the protein subsequently isolated and administered exogenously to subjects who would benefit therefrom, or in vivo, i.e., administration by gene therapy. Naturally, any DNA encoding the same protein may be used for the same purpose, and a DNA encoding a protein which a fragment or a mutant of that naturally occurring protein which retains the desired activity, may be used for the purpose of producing the active fragment or mutant. The encoded protein of course has utility therapeutically and, in labeled or immobilized form, diagnostically.

The genes may also be used indirectly, that is, to identify other useful DNAs, proteins, or other molecules. We have attempted to determine whether the mouse genes disclosed herein have significant similarity to any known human DNA, and whether, in any of the six possible combinations of reference frame and strand, they encode a protein similar to a known human protein. If so, then it

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follows that the known human protein, and DNAs encoding that protein, may be used in a similar manner. In addition, if the known human protein is known to have additional homologues, then those homologous proteins, and DNAs encoding them, may be used in a similar marner.

There thus are several ways that a human protein homologue of interest can be identified by database searching, including but not limited to:

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- 1) a DNA->DNA (BlastN) search for human database DNAs closely related to the mouse gene identifies a known human gene, and the sequence of the human protein is deduced by the Genetic Code;
- 2) a DNA->Protein (BlastX) search for humn database proteins closely related to the translated DNA of the mouse gene identifies a known human protein; and
- 3) the sequence of the mouse protein is known or is deduced by the Genetic Code, and a Protein->Protein (BlastP) search for closely related database proteins identifies a known human protein.

Once a known human gene is identified, it may be used in further BlastN or BlastX searches to identify other human genes or proteins. Once a known human protein is identified, it may be used in further BlastP searches to identify other human proteins.

Searches may also take cognizance, intermediately, of known genes and proteins other than mouse or human ones, e.g., use the mouse sequence to identify a known rat sequence and then the rat sequence to identify a human one.

If we have identified a mouse gene, and it encodes a mouse protein which appears similar to a human protein, then that human protein may be used (especially in humans) for

purposes analogous to the proposed use of the mouse protein in mice. Moreover, a specific binding fragment of an appropriate strand of the corresponding human gene (gDNA or cDNA) could be labeled and used as a hybridization probe (especially against samples of human mRNA or cDNA).

In determining whether the disclosed genes (gDNA or cDNA) have significant similarities to known DNAs (and their translated AA sequences to known proteins), one would generally use the disclosed gene as a query sequence in a search of a sequence database. The results of several such searches are set forth in the Examples. Such results are dependent, to some degree, on the search parameters. Preferred parameters are set forth in Example 1. The results are also dependent on the content of the database. While the raw similarity score of a particular target (database) sequence will not vary with content (as long as it remains in the database), its informational value (in bits), expected value, and relative ranking can change. Generally speaking, the changes are small.

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It will be appreciated that the nucleic acid and protein databases keep growing. Hence a later search may identify high scoring target sequences which were not uncovered by an earlier search because the target sequences were not previously part of a database.

Hence, in a preferred embodiment, the cognate DNAs and proteins include not only those set forth in the examples, but those which would have been highly ranked (top ten, more preferably top three, even more preferably top two, most preferably the top one) in a search run with the same parameters on the date of filing of this application.

If the known mouse or human database DNA appears to be a partial sequence (that is, partial relative to a cDNA or gDNA encoding the whole naturally occurring protein), it may be used as a hybridization probe to isolate the full-length DNA. If the partial DNA encodes a biologically functional fragment of the cognate protein, it may be used in a manner

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similar to the full length DNA, i.e., to produce the functional fragment.

If we have indicated that an antagonist of a protein or other molecule is useful, then such an antagonist may be obtained by preparing a combinatorial library, as described below, of potential antagonists, and screening the library members for binding to the protein or other molecule in question. The binding members may then be further screened for the ability to antagonize the biological activity of the target. The antagonists may be used therapeutically, or, in suitably labeled or immobilized form, diagnostically.

If the identified mouse or human database DNA is related to a known protein, then substances known to interact with that protein (e.g., agonists, antagonists, substrates, receptors, second messengers, regulators, and so forth), and binding molecules which bind them, are also of utility. Such binding molecules can likewise be identified by screening a combinatorial library.

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Isolation of Full Length DNAs Using Partial DNAs as probes

If it is determined that a DNA of the present invention is a partial DNA, and the cognate full length DNA is not listed in a sequence database, the available DNA may be used as a hybridization probe to isolate the full-length DNA from a suitable DNA library.

Stringent hybridization conditions are appropriate, that is, conditions in which the hybridization temperature is 5-10 deg. C. below the Tm of the DNA as a perfect duplex.

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Identification and Isolation of Homologous Genes Using a DNA Probe

It may be that the sequence databases available do not include the sequence of any homologous gene (cDNA or gDNA), or at least of the homologous gene for a species of interest. However, given the cDNAs set forth above, one may readily obtain the homologous gene.

The possession of one DNA (the "starting DNA") greatly facilitates the isolation of homologous DNAs. If only a

partial DNA is known, this partial DNA may first be used as a probe to isolate the corresponding full length DNA for the same species, and that the latter may be used as the starting DNA in the search for homologous genes.

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The starting DNA, or a fragment thereof, is used as a hybridization probe to screen a cDNA or genomic DNA library for clones containing inserts which encode either the entire homologous protein, or a recognizable fragment thereof. The minimum length of the hybridization probe is dictated by the need for specificity. If the size of the library in bases is L, and the GC content is 50%, then the probe should have a length of at least 1, where $L=4^1$. This will yield, on average, a single perfect match in random DNA of L bases. The human cDNA library is about 10^8 bases and the human genomic DNA library is about 10^{10} bases.

The library is preferably derived from an organism which is known, on biochemical evidence, to produce a homologous protein, and more preferably from the genomic DNA or mRNA of cells of that organism which are likely to be relatively high producers of that protein. A cDNA library (which is derived from an mRNA library) is especially preferred.

If the organism in question is known to have substantially different codon preferences from that of the organism whose relevant cDNA or genomic DNA is known, a synthetic hybridization probe may be used which encodes the same amino acid sequence but whose codon utilization is more similar to that of the DNA of the target organism. Alternatively, the synthetic probe may employ inosine as a substitute for those bases which are most likely to be divergent, or the probe may be a mixed probe which mixes the codons for the source DNA with the preferred codons (encoding the same amino acid) for the target organism.

By routine methods, the Tm of a perfect duplex of starting DNA is determined. One may then select a hybridization temperature which is sufficiently lower than the perfect duplex Tm to allow hybridization of the starting DNA (or other probe) to a target DNA which is divergent from the starting DNA. A 1% sequence divergence typically lowers

the Tm of a duplex by 1-2°C, and the DNAs encoding homologous proteins of different species typically have sequence identities of around 50-80%. Preferably, the library is screened under conditions where the temperature is at least 20°C., more preferably at least 50°C., below the perfect duplex Tm. Since salt reduces the Tm, one ordinarily would carry out the search for DNAs encoding highly homologous proteins under relatively <u>low</u> salt hybridization conditions, e.g., <1M NaCl. The higher the salt concentration, and/or the lower the temperature, the greater the sequence divergence which is tolerated.

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For the use of probes to identify homologous genes in other species, see, e.g., Schwinn, et al., J. Biol. Chem., 265:8183-89 (1990) (hamster 67-bp cDNA probe vs. human leukocyte genomic library; human 0.32kb DNA probe vs. bovine brain cDNA library, both with hybridization at 42°C in 6xSSC); Jenkins et al., J. Biol. Chem., 265:19624-31 (1990) (Chicken 770-bp cDNA probe vs. human genomic libraries; hybridization at 40°C in 50% formamide and 5xSSC); Murata et al., J. Exp. Med., 175:341-51 (1992) (1.2-kb mouse cDNA probe v. human eosinophil cDNA library; hybridization at 65°C in 6xSSC); Guyer et al., J. Biol. Chem., 265:17307-17 (1990) (2.95-kb human genomic DNA probe vs. porcine genomic DNA library; hybridization at 42°C in 5xSSC). The conditions set forth in these articles may each be considered suitable for the purpose of isolating homologous genes.

Corresponding (Homologous) Proteins and DNAs

In the case of a gene chip, the manufacturer of the gene chip determines which DNA to place at each position on the chip. This DNA may correspond in sequence to a genomic DNA, a cDNA, or a fragment of genomic or cDNA, and may be natural, synthetic or partially natural and partially synthetic in origin. The manufacturer of the gene chip will normally identify the DNA for a mouse gene chip as corresponding to a particular mouse gene, in which case it will be assumed that the alignments of chip DNA to mouse gene satisfies the homology criteria of the invention.

Usually, the gene chip manufacturer will provide a sequence database accession number for the mouse DNA. If so, to identify the corresponding mouse protein, we will first inspect the database record for that mouse DNA. Often, the mouse protein accession number will appear in that record or in a linked record. If it doesn't, the corresponding mouse protein can be identified by performing a BlastX search on a mouse protein database with the mouse database DNA sequence as the query sequence. Even if the protein sequence is not in the database, if the DNA sequence comprises a full-length coding sequence, the corresponding protein can be identified by translating the coding sequence in accordance with the Genetic Code.

A human protein can be said to be identifiable as corresponding (homologous) to a gene chip DNA if it is identified as corresponding (homologous) to the mouse gene (gDNA or cDNA, whole or partial) identified by the gene chip manufacturer as corresponding to that gene chip DNA.

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In turn, it is identifiable as corresponding (homologous) to said identified mouse gene, if

- (1) it can be aligned by BlastX directly to that mouse gene, and/or
- (2) it is encoded by a human gene, or can be aligned to a human gene by BlastX, which in turn can be aligned by BlastN to said mouse gene and/or
- (3) it can be aligned by BlastP to a mouse protein, the latter being encoded by said mouse gene, or aligned to said mouse gene BlastX,
- where any alignment by BlastN, BlastP or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone)

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is less than e-10. (Note that because this is a negative exponent, a value such as e-50 is less than e-10.)

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Desirably, two or all three of these conditions (1)-(3) are satisfied for the corresponding (homologous) human genes and proteins.

A human gene is corresponding (homologous) to a mouse gene chip DNA, and hence to said identified mouse gene (or cDNA) and protein, if it encodes a corresponding (homologous) human protein as defined above, or it can be aligned by BlastN to said mouse gene.

Preferably, for at least one of conditions (1)-(3), the E value is less than e-50, more preferably less than e-60, still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100. Desirably, it is true for two or even all three of these conditions.

In constructing Master table 1, we generally used a BlastX (mouse gene vs. human protein) alignment E value cutoff of e-50. However, if there were no human proteins with that good an alignment to the mouse DNA in question, or if there were other reasons for including a particular human protein (e.g., a known functionality supportive of the observed differential cognate mouse protein expression), then a human protein with a score worse (i.e., higher) than e-50 may appear in Master Table 1.

If the manufacturer of the gene chip identifies the gene chip DNA as corresponding to an EST, or other DNA which is not a full-length mouse gene or cDNA, a longer (possibly full length) mouse gene or cDNA may be identified by a BlastN search of the mouse DNA database. Alternatively, the identified DNA may be used to conduct a BlastN search of a human DNA database, or a BlastX search of a mouse or human protein database.

Thus, more generally, a human protein can be said to be identifiable as corresponding (homologous) to a gene chip

DNA, or to a DNA identified by the manufacturer as corresponding to that gene chip DNA, if

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- (1') it can be aligned directly to the gene chip or corresponding manufacturer identified DNA by BlastX. and/or
 - (2') it can be aligned to a human gene/cDNA by BlastX, whose genomic DNA (gDNA) or cDNA (DNA complementary to messenger RNA) in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or
 - (3') it can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or
- (4') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastX, and/or
- (5') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA can in turn be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN;
- where any alignment by BlastN, BlastP, or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone) is less than e-10. (Note that because this is a negative exponent, a value such as e-50 is less than e-10.)

Preferably, two, three, four or all five of conditions (1')-(5') are satisfied.

Preferably, for at least one of conditions (1')-(5'), for at least the final alignment (i.e., vs. the human protein), the E value is less than e-50, more preferably less than e-60, still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100.

Desirably, one or more of these standards of preference are met for two, three, four or all five of conditions (1')-(5'). In particular, for those conditions in which the gene chip or corresponding manufacturer identified DNA is indirectly connected to the human protein by virtue of two or more successive alignments, the E value is preferably, so limited for all of said alignments in the connecting chain.

A human gene corresponds (is homologous) to a gene chip DNA or manufacturer identified corresponding DNA if it encodes a homologous human protein as defined above, or if it can be aligned either directly to that DNA, or indirectly through a mouse gene which can be aligned to said DNA, according to the conditions set forth above.

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Master table 1 assembles a list of human protein corresponding to each of the mouse DNAs/proteins identified as related to the chip DNA. These human proteins form a set and can be given a percentile rank, with respect to E value, within that set. The human proteins of the present invention preferably are those scorers with a percentile rank of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

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For each mouse gene (gDNA or cDNA) in Master Table 1, there is a particular human protein which provides the best alignment match as measured by BlastX, i.e., the human protein with the best score (lowest e-value). These human proteins form a subset of the set above and can be given a percentile rank within that subset, e.g., the human proteins with scores in the top 10% of that subset have a percentile rank of 90% or higher.

The human proteins of the present invention preferably are those best scorer subset proteins with a percentile rank within the subset of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

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BlastN and BlastX report very low expected values as "0.0". This does not truly mean that the expected value is exactly zero (since any alignment could occur by chance), but merely that it is so infinitesimal that it is not reported. The documentation does not state the cutoff value, but alignments with explicit E values as low as e-178 (624 bits) have been reported as nonzero values, while a score of 636 bits was reported as "0.0".

Functionally homologous human proteins are also of interest. A human protein may be said to be functionally homologous to the mouse gene if the human protein has at least one biological activity in common with the mouse protein encoded by said mouse gene.

The human proteins of interest also include those that are substantially and/or conservatively identical (as defined below) to the homologous and/or functionally homologous human proteins defined above.

Degree of Differential Expression

The degree of differential expression may be expressed as the ratio of the higher expression level to the lower expression level. Preferably, this is at least 2-fold, and more preferably, it is higher, such as at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold.

Most preferably, the human protein of interest corresponds to a mouse gene for which the degree of differential expression places it among the top 10% of the mouse genes in the appropriate subtable.

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If a gene is down-regulated in more favored mammals, or up-regulated in less favored mammals, (i.e., an "unfavorable gene") then several utilities are apparent.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Elevated levels are indicative of progression, or propensity to progression, to a less favored state, and clinicians may take appropriate preventative, curative or ameliorative action.

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Secondly, the messenger RNA product (or equivalent cDNA), the protein product, or a binding molecule specific for that product (e.g., an antibody which binds the product), or a downstream product which mediates the activity (e.g., a signaling intermediate) or a binding molecule (e.g., an antibody) therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said nucleic acid product, protein product, or downstream product (e.g., a signaling intermediate). Again, elevated levels are indicative of a present or future problem.

Thirdly, an agent which down-regulates expression of the gene may be used to reduce levels of the corresponding protein and thereby inhibit further damage. This agent could inhibit transcription of the gene in the subject, or translation of the corresponding messenger RNA. Possible inhibitors of transcription and translation include antisense molecules and repressor molecules. The agent could also inhibit a post-translational modification (e.g., glycosylation, phosphorylation, cleavage, GPI attachment) required for activity, or post-translationally modify the protein so as to inactivate it. Or it could be an agent which down- or up-regulated a positive or negative regulatory gene, respectively.

Fourthly, an agent which is an antagonist of the messenger RNA product or protein product of the gene, or of a downstream product through which its activity is

manifested (e.g., a signaling intermediate), may be used to inhibit its activity.

This antagonist could be an antibody, a peptide, a peptoid, a nucleic acid, a peptide nucleic acid (PNA) oligomer, a small organic molecule of a kind for which a combinatorial library exists (e.g., a benzodiazepine), etc. An antagonist is simply a binding molecule which, by binding, reduces or abolishes the undesired activity of its target. The antagonist, if not an oligomeric molecule, is preferably less than 1000 daltons, more preferably less than 500 daltons.

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Fifthly, an agent which degrades, or abets the degradation of, that messenger RNA, its protein product or a downstream product which mediates its activity (e.g., a signaling intermediate), may be used to curb the effective period of activity of the protein.

If a gene is <u>up</u>-regulated in more favored mammals, or <u>down</u>-regulated in less favored animals then the utilities are converse to those stated above.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Depressed levels are indicative of damage, or possibly of a propensity to damage, and clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product, the equivalent cDNA, protein product, or a binding molecule specific for those products, or a downstream product, or a signaling intermediate, or a binding molecule therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said protein product or downstream product. Again, depressed levels are indicative of a present or future problem.

Thirdly, an agent which up-regulates expression of the gene may be used to increase levels of the corresponding protein and thereby inhibit further progression to a less favored state. By way of example, it could be a vector which carries a copy of the gene, but which expresses the

gene at higher levels than does the endogenous expression system. Or it could be an agent which up- or down-regulates a positive or negative regulatory gene.

Fourthly, an agent which is an agonist of the protein product of the gene, or of a downstream product through which its activity (of inhibition of progression to a less favored state) is manifested, or of a signaling intermediate may be used to foster its activity.

Fifthly, an agent which inhibits the degradation of that protein product or of a downstream product or of a signaling intermediate may be used to increase the effective period of activity of the protein.

Mutant Proteins

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The present invention also contemplates mutant proteins (peptides) which are substantially identical (as defined below) to the parental protein (peptide). In general, the fewer the mutations, the more likely the mutant protein is to retain the activity of the parental protein. The effect of mutations is usually (but not always) additive. Certain individual mutations are more likely to be tolerated than others.

A protein is more likely to tolerate a mutation which

- (a) is a substitution rather than an insertion or deletion;
- (b) is an insertion or deletion at the terminus, rather than internally, or, if internal, is at a domain boundary, or a loop or turn, rather than in an alpha helix or beta strand;
- (c) affects a surface residue rather than an interior residue;
- (d) affects a part of the molecule distal to the binding site;
- (e) is a substitution of one amino acid for another of similar size, charge, and/or hydrophobicity, and does not destroy a disulfide bond or other crosslink; and

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(f) is at a site which is subject to substantial variation among a family of homologous proteins to which the protein of interest belongs.

These considerations can be used to design functional mutants.

Surface vs. Interior Residues

Charged amino acid residues almost always lie on the surface of the protein. For uncharged residues, there is less certainty, but in general, hydrophilic residues are partitioned to the surface and hydrophobic residues to the interior. Of course, for a membrane protein, the membrane-spanning segments are likely to be rich in hydrophobic residues.

Surface residues may be identified experimentally by various labeling techniques, or by 3-D structure mapping techniques like X-ray diffraction and NMR. A 3-D model of a homologous protein can be helpful.

20 Binding Site Residues

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Residues forming the binding site may be identified by (1) comparing the effects of labeling the surface residues before and after complexing the protein to its target, (2) labeling the binding site directly with affinity ligands, (3) fragmenting the protein and testing the fragments for binding activity, and (4) systematic mutagenesis (e.g., alanine-scanning mutagenesis) to determine which mutants destroy binding. If the binding site of a homologous protein is known, the binding site may be postulated by analogy.

Protein libraries may be constructed and screened that a large family (e.g., 108) of related mutants may be evaluated simultaneously.

Hence, the mutations are preferably conservative modifications as defined below.

"Substantially Identical"

A mutant protein (peptide) is substantially identical to a reference protein (peptide) if (a) it has at least 10%

of a specific binding activity or a non-nutritional biological activity of the reference protein, and (b) is at least 50% identical in amino acid sequence to the reference protein (peptide). It is "substantially structurally identical" if condition (b) applies, regardless of (a).

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Percentage amino acid identity is determined by aligning the mutant and reference sequences according to a rigorous dynamic programming algorithm which globally aligns their sequences to maximize their similarity, the similarity being scored as the sum of scores for each aligned pair according to an unbiased PAM250 matrix, and a penalty for each internal gap of -12 for the first null of the gap and -4 for each additional null of the same gap. The percentage identity is the number of matches expressed as a percentage of the adjusted (i.e., counting inserted nulls) length of the reference sequence.

A mutant DNA sequence is substantially identical to a reference DNA sequence if they are structural sequences, and encoding mutant and reference proteins which are substantially identical as described above.

If instead they are regulatory sequences, they are substantially identical if the mutant sequence has at least 10% of the regulatory activity of the reference sequence, and is at least 50% identical in nucleotide sequence to the reference sequence. Percentage identity is determined as for proteins except that matches are scored +5, mismatches -4, the gap open penalty is -12, and the gap extension penalty (per additional null) is -4.

More preferably, the sequence is not merely substantially identical but rather is at least 51%, at least 66%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical in sequence to the reference sequence.

DNA sequences may also be considered "substantially identical" if they hybridize to each other under stringent conditions, i.e., conditions at which the Tm of the heteroduplex of the one strand of the mutant DNA and the more complementary strand of the reference DNA is not in

excess of 10°C. less than the Tm of the reference DNA homoduplex. Typically this will correspond to a percentage identity of 85-90%.

5 "Conservative Modifications"

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"Conservative modifications" are defined as

- (a) conservative substitutions of amino acids as hereafter defined; or
- (b) single or multiple insertions (extension) or deletions (truncation) of amino acids at the termini.

Conservative modifications are preferred to other modifications. Conservative substitutions are preferred to other conservative modifications.

"Semi-Conservative Modifications" are modifications which are not conservative, but which are (a) semi-conservative substitutions as hereafter defined; or (b) single or multiple insertions or deletions internally, but at interdomain boundaries, in loops or in other segments of relatively high mobility. Semi-conservative modifications are preferred to nonconservative modifications. Semi-conservative substitutions are preferred to other semi-conservative modifications.

Non-conservative substitutions are preferred to other non-conservative modifications.

The term "conservative" is used here in an <u>a priori</u> sense, i.e., modifications which would be <u>expected</u> to preserve 3D structure and activity, based on analysis of the naturally occurring families of homologous proteins and of past experience with the effects of deliberate mutagenesis, rather than <u>post facto</u>, a modification already known to conserve activity. Of course, a modification which is conservative <u>a priori</u> may, and usually is, also conservative <u>post facto</u>.

Preferably, except at the termini, no more than about five amino acids are inserted or deleted at a particular locus, and the modifications are outside regions known to contain binding sites important to activity.

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Preferably, insertions or deletions are limited to the termini.

A conservative substitution is a substitution of one amino acid for another of the same exchange group, the exchange groups being defined as follows

- I Gly, Pro, Ser, Ala (Cys) (and any nonbiogenic, neutral amino acid with a hydrophobicity not exceeding that of the aforementioned a.a.'s)
- II Arg, Lys, His (and any nonbiogenic, positively-charged amino acids)
- III Asp, Glu, Asn, Gln (and any nonbiogenic
 negatively-charged amino acids)
- IV Leu, Ile, Met, Val (Cys) (and any nonbiogenic, aliphatic, neutral amino acid with a hydrophobicity too high for I above)
- V Phe, Trp, Tyr (and any nonbiogenic, aromatic neutral amino acid with a hydrophobicity too high for I above).

Note that Cys belongs to both I and IV.

Residues Pro, Gly and Cys have special conformational roles. Cys participates in formation of disulfide bonds. Gly imparts flexibility to the chain. Pro imparts rigidity to the chain and disrupts α helices. These residues may be essential in certain regions of the polypeptide, but substitutable elsewhere.

One, two or three conservative substitutions are more likely to be tolerated than a larger number.

"Semi-conservative substitutions" are defined herein as being substitutions within supergroup I/II/III or within supergroup IV/V, but not within a single one of groups I-V. They also include replacement of any other amino acid with alanine. If a substitution is not conservative, it preferably is semi-conservative.

"Non-conservative substitutions" are substitutions which are not "conservative" or "semi-conservative".

"Highly conservative substitutions" are a subset of conservative substitutions, and are exchanges of amino acids within the groups Phe/Tyr/Trp, Met/Leu/Ile/Val, His/Arg/Lys, Asp/Glu and Ser/Thr/Ala. They are more likely to be

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tolerated than other conservative substitutions. Again, the smaller the number of substitutions, the more likely they are to be tolerated.

"Conservatively Identical"

A protein (peptide) is conservatively identical to a reference protein (peptide) it differs from the latter, if at all, solely by conservative modifications, the protein (peptide remaining at least seven amino acids long if the reference protein (peptide) was at least seven amino acids long.

A protein is at least semi-conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by semi-conservative or conservative modifications.

A protein (peptide) is nearly conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by one or more conservative modifications and/or a single nonconservative substitution.

It is highly conservatively identical if it differs, if at all, solely by highly conservative substitutions. Highly conservatively identical proteins are preferred to those merely conservatively identical. An absolutely identical protein is even more preferred.

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The core sequence of a reference protein (peptide) is the largest single fragment which retains at least 10% of a particular specific binding activity, if one is specified, or otherwise of at least one specific binding activity of the referent. If the referent has more than one specific binding activity, it may have more than one core sequence, and these may overlap or not.

If it is taught that a peptide of the present invention may have a particular similarity relationship (e.g., markedly identical) to a reference protein (peptide), preferred peptides are those which comprise a sequence having that relationship to a core sequence of the reference protein (peptide), but with internal insertions or deletions

in either sequence excluded. Even more preferred peptides are those whose entire sequence has that relationship, with the same exclusion, to a core sequence of that reference protein (peptide).

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Library

The term "library" generally refers to a collection of chemical or biological entities which are related in origin, structure, and/or function, and which can be screened simultaneously for a property of interest.

Libraries may be classified by how they are constructed (natural vs. artificial diversity; combinatorial vs. noncombinatorial), how they are screened (hybridization, expression, display), or by the nature of the screened library members (peptides, nucleic acids, etc.).

In a "natural diversity" library, essentially all of the diversity arose without human intervention. This would be true, for example, of messenger RNA extracted from a nonengineered cell.

In a "synthetic diversity" library, essentially all of the diversity arose deliberately as a result of human intervention. This would be true for example of a combinatorial library; note that a small level of natural diversity could still arise as a result of spontaneous mutation. It would also be true of a noncombinatorial library of compounds collected from diverse sources, even if they were all natural products.

In a "non-natural diversity" library, at least some of the diversity arose deliberately through human intervention.

In a "controlled origin" library, the source of the diversity is limited in some way. A limitation might be to cells of a particular individual, to a particular species, or to a particular genus, or, more complexly, to individuals of a particular species who are of a particular age, sex, physical condition, geographical location, occupation and/or familial relationship. Alternatively or additionally, it might be to cells of a particular tissue or organ. Or it could be cells exposed to particular pharmacological,

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environmental, or pathogenic conditions. Or the library could be of chemicals, or a particular class of chemicals, produced by such cells.

In a "controlled structure" library, the library members are deliberately limited by the production conditions to particular chemical structures. For example, if they are oligomers, they may be limited in length and monomer composition, e.g. hexapeptides composed of the twenty genetically encoded amino acids.

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Hybridization Library

In a hybridization library, the library members are nucleic acids, and are screened using a nucleic acid hybridization probe. Bound nucleic acids may then be amplified, cloned, and/or sequenced.

Expression Library

In an expression library, the screened library members are gene expression products, but one may also speak of an underlying library of genes encoding those products. The library is made by subcloning DNA encoding the library members (or portions thereof) into expression vectors (or into cloning vectors which subsequently are used to construct expression vectors), each vector comprising an expressible gene encoding a particular library member, introducing the expression vectors into suitable cells, and expressing the genes so the expression products are produced.

In one embodiment, the expression products are secreted, so the library can be screened using an affinity reagent, such as an antibody or receptor. The bound expression products may be sequenced directly, or their sequences inferred by, e.g., sequencing at least the variable portion of the encoding DNA.

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In a second embodiment, the cells are lysed, thereby exposing the expression products, and the latter are screened with the affinity reagent.

In a third embodiment, the cells express the library members in such a manner that they are displayed on the

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surface of the cells, or on the surface of viral particles produced by the cells. (See display libraries, below).

In a fourth embodiment, the screening is not for the ability of the expression product to bind to an affinity reagent, but rather for its ability to alter the phenotype of the host cell in a particular detectable manner. Here, the screened library members are transformed cells, but there is a first underlying library of expression products which mediate the behavior of the cells, and a second underlying library of genes which encode those products.

Display Library

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In a display library, the library members are each conjugated to, and displayed upon, a support of some kind. The support may be living (a cell or virus), or nonliving (e.g., a bead or plate).

If the support is a cell or virus, display will normally be effectuated by expressing a fusion protein which comprises the library member, a carrier moiety allowing integration of the fusion protein into the surface of the cell or virus, and optionally a lining moiety. In a variation on this theme, the cell coexpresses a first fusion comprising the library member and a linking moiety L1, and a second fusion comprising a linking moiety L2 and the carrier moiety. L1 and L2 interact to associate the first fusion with the second fusion and hence, indirectly, the library member with the surface of the cell or virus.

Soluble Library

In a soluble library, the library members are free in solution. A soluble library may be produced directly, or one may first make a display library and then release the library members from their supports.

Encapsulated Library

In an encapsulated library, the library members are inside cells or liposomes. Generally speaking, encapsulated libraries are used to store the library members for future use; the members are extracted in some way for screening

purposes. However, if they differentially affect the phenotype of the cells, they may be screened indirectly by screening the cells.

5 <u>cDNA Library</u>

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A cDNA library is usually prepared by extracting RNA from cells of particular origin, fractionating the RNA to isolate the messenger RNA (mRNA has a poly(A) tail, so this is usually done by oligo-dT affinity chromatography), synthesizing complementary DNA (cDNA) using reverse transcriptase, DNA polymerase, and other enzymes, subcloning the cDNA into vectors, and introducing the vectors into cells. Often, only mRNAs or cDNAs of particular sizes will be used, to make it more likely that the cDNA encodes a functional polypeptide.

A cDNA library explores the natural diversity of the transcribed DNAs of cells from a particular source. It is not a combinatorial library.

A cDNA library may be used to make a hybridization library, or it may be used as an (or to make) expression library.

Genomic DNA Library

A genomic DNA library is made by extracting DNA from a particular source, fragmenting the DNA, isolating fragments of a particular size range, subcloning the DNA fragments into vectors, and introducing the vectors into cells.

Like a cDNA library, a genomic DNA library is a natural diversity library, and not a combinatorial library. A genomic DNA library may be used the same way as a cDNA library.

Synthetic DNA library

A synthetic DNA library may be screened directly (as a hybridization library), or used in the creation of an expression or display library of peptides/proteins.

Combinatorial Libraries

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The term "combinatorial library" refers to a library in which the individual members are either systematic or random combinations of a limited set of basic elements, the properties of each member being dependent on the choice and location of the elements incorporated into it. Typically, the members of the library are at least capable of being screened simultaneously. Randomization may be complete or partial; some positions may be randomized and others predetermined, and at random positions, the choices may be limited in a predetermined manner. The members of a combinatorial library may be oligomers or polymers of some kind, in which the variation occurs through the choice of monomeric building block at one or more positions of the oligomer or polymer, and possibly in terms of the connecting linkage, or the length of the oligomer or polymer, too. Or the members may be nonoligomeric molecules with a standard core structure, like the 1,4-benzodiazepine structure, with the variation being introduced by the choice of substituents at particular variable sites on the core structure. members may be nonoligomeric molecules assembled like a jigsaw puzzle, but wherein each piece has both one or more variable moieties (contributing to library diversity) and one or more constant moieties (providing the functionalities for coupling the piece in question to other pieces).

Thus, in a typical combinatorial library, chemical building blocks are at least partially randomly combined into a large number (as high as 10¹⁵) of different compounds, which are then simultaneously screened for binding (or other) activity against one or more targets.

In a "simple combinatorial library", all of the members belong to the same class of compounds (e.g., peptides) and can be synthesized simultaneously. A "composite combinatorial library" is a mixture of two or more simple libraries, e.g., DNAs and peptides, or peptides, peptoids, and PNAs, or benzodiazepines and carbamates. The number of component simple libraries in a composite library will, of course, normally be smaller than the average number of members in each simple library, as otherwise the advantage of a library over individual synthesis is small.

Libraries of thousands, even millions, of random oligopeptides have been prepared by chemical synthesis (Houghten et al., Nature, 354:84-6(1991)), or gene expression (Marks et al., J Mol Biol, 222:581-97(1991)), displayed on chromatographic supports (Lam et al., Nature, 354:82-4(1991)), inside bacterial cells (Colas et al., Nature, 380:548-550 (1996)), on bacterial pili (Lu, Bio/Technology, 13:366-372(1990)), or phage (Smith, Science, 228:1315-7(1985)), and screened for binding to a variety of targets including antibodies (Valadon et al., J Mol Biol, 261:11-22(1996)), cellular proteins (Schmitz et al., J Mol Biol, 260:664-677(1996)), viral proteins (Hong and Boulanger, Embo J, 14:4714-4727(1995)), bacterial proteins (Jacobsson and Frykberg, Biotechniques, 18:878-885(1995)), nucleic acids (Cheng et al., Gene, 171:1-8(1996)), and plastic (Siani et al., J Chem Inf Comput Sci, 34:588-593 (1994)).

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Libraries of proteins (Ladner, USP 4,664,989), peptoids (Simon et al., Proc Natl Acad Sci U S A, 89:9367-71(1992)), nucleic acids (Ellington and Szostak, Nature, 246:818(1990)), carbohydrates, and small organic molecules (Eichler et al., Med Res Rev, 15:481-96(1995)) have also been prepared or suggested for drug screening purposes.

The first combinatorial libraries were composed of peptides or proteins, in which all or selected amino acid positions were randomized. Peptides and proteins can exhibit high and specific binding activity, and can act as catalysts. In consequence, they are of great importance in biological systems.

Nucleic acids have also been used in combinatorial libraries. Their great advantage is the ease with which a nucleic acid with appropriate binding activity can be amplified. As a result, combinatorial libraries composed of nucleic acids can be of low redundancy and hence, of high diversity.

There has also been much interest in combinatorial libraries based on small molecules, which are more suited to pharmaceutical use, especially those which, like benzodiazepines, belong to a chemical class which has

already yielded useful pharmacological agents. The techniques of combinatorial chemistry have been recognized as the most efficient means for finding small molecules that act on these targets. At present, small molecule combinatorial chemistry involves the synthesis of either pooled or discrete molecules that present varying arrays of functionality on a common scaffold. These compounds are grouped in libraries that are then screened against the target of interest either for binding or for inhibition of biological activity.

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The size of a library is the number of molecules in it. The simple diversity of a library is the number of unique structures in it. There is no formal minimum or maximum diversity. If the library has a very low diversity, the library has little advantage over just synthesizing and screening the members individually. If the library is of very high diversity, it may be inconvenient to handle, at least without automatizing the process. The simple diversity of a library is preferably at least 10, 10E2, 10E3, 10E4, 10E6, 10E7, 10E8 or 10E9, the higher the better under most circumstances. The simple diversity is usually not more than 10E15, and more usually not more than 10E10.

The average sampling level is the size divided by the simple diversity. The expected average sampling level must be high enough to provide a reasonable assurance that, if a given structure were expected, as a consequence of the Library design, to be present, that the actual average sampling level will be high enough so that the structure, if satisfying the screening criteria, will yield a positive result when the library is screened. Thus, the preferred average sampling level is a function of the detection limit, which in turn is a function of the strength of the signal to be screened.

There are more complex measures of diversity than simple diversity. These attempt to take into account the degree of structural difference between the various unique sequences. These more complex measures are usually used in the context of small organic compound libraries, see below.

The library members may be presented as solutes in solution, or immobilized on some form of support. In the latter case, the support may be living (cell, virus) or nonliving (bead, plate, etc.). The supports may be separable (cells, virus particles, beads) so that binding and nonbinding members can be separated, or nonseparable (plate). In the latter case, the members will normally be placed on addressable positions on the support. The advantage of a soluble library is that there is no carrier moiety that could interfere with the binding of the members to the support. The advantage of an immobilized library is that it is easier to identify the structure of the members which were positive.

When screening a soluble library, or one with a separable support, the target is usually immobilized. When screening a library on a nonseparable support, the target will usually be labeled.

Oligonucleotide Libraries

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An oligonucleotide library is a combinatorial library, at least some of whose members are single-stranded oligonucleotides having three or more nucleotides connected by phosphodiester or analogous bonds. The oligonucleotides may be linear, cyclic or branched, and may include non-nucleic acid moieties. The nucleotides are not limited to the nucleotides normally found in DNA or RNA. For examples of nucleotides modified to increase nuclease resistance and chemical stability of aptamers, see Chart 1 in Osborne and Ellington, Chem. Rev., 97: 349-70 (1997). For screening of RNA, see Ellington and Szostak, Nature, 346: 818-22 (1990).

There is no formal minimum or maximum size for these oligonucleotides. However, the number of conformations which an oligonucleotide can assume increases exponentially with its length in bases. Hence, a longer oligonucleotide is more likely to be able to fold to adapt itself to a protein surface. On the other hand, while very long molecules can be synthesized and screened, unless they provide a much superior affinity to that of shorter molecules, they are not likely to be found in the selected population, for the

reasons explained by Osborne and Ellington (1997). Hence, the libraries of the present invention are preferably composed of oligonucleotides having a length of 3 to 100 bases, more preferably 15 to 35 bases. The oligonucleotides in a given library may be of the same or of different lengths.

Oligonucleotide libraries have the advantage that libraries of very high diversity (e.g., 10¹⁵) are feasible, and binding molecules are readily amplified in vitro by polymerase chain reaction (PCR). Moreover, nucleic acid molecules can have very high specificity and affinity to targets.

In a preferred embodiment, this invention prepares and screens oligonucleotide libraries by the SELEX method, as described in King and Famulok, Molec. Biol. Repts., 20: 97-107 (1994); L. Gold, C. Tuerk. Methods of producing nucleic acid ligands, US#5595877; Oliphant et al. Gene 44:177 (1986).

The term "aptamer" is conferred on those oligonucleotides which bind the target protein. Such aptamers may be used to characterize the target protein, both directly (through identification of the aptamer and the points of contact between the aptamer and the protein) and indirectly (by use of the aptamer as a ligand to modify the chemical reactivity of the protein).

In a classic oligonuclotide, each nucleotide (monomeric unit) is composed of a phosphate group, a sugar moiety, and either a purine or a pyrimidine base. In DNA, the sugar is deoxyribose and in RNA it is ribose. The nucleotides are linked by 5'-3' phosphodiester bonds.

The deoxyribose phosphate backbone of DNA can be modified to increase resistance to nuclease and to increase penetration of cell membranes. Derivatives such as mono- or dithiophosphates, methyl phosphonates, boranophosphates, formacetals, carbamates, siloxanes, and dimethylenethio-sulfoxideo- and-sulfono- linked species are known in the art.

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A peptide is composed of a plurality of amino acid residues joined together by peptidyl (-NHCO-) bonds. A biogenic peptide is a peptide in which the residues are all genetically encoded amino acid residues; it is not necessary that the biogenic peptide actually be produced by gene expression.

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Amino acids are the basic building blocks with which peptides and proteins are constructed. Amino acids possess both an amino group $(-NH_2)$ and a carboxylic acid group (-COOH). Many amino acids, but not all, have the alpha amino acid structure NH_2 -CHR-COOH, where R is hydrogen, or any of a variety of functional groups.

Twenty amino acids are genetically encoded: Alanine, Arginine, Asparagine, Aspartic Acid, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, and Valine. Of these, all save Glycine are optically isomeric, however, only the L-form is found in humans. Nevertheless, the D-forms of these amino acids do have biological significance; D-Phe, for example, is a known analgesic.

Many other amino acids are also known, including: 2Aminoadipic acid; 3-Aminoadipic acid; beta-Aminopropionic
acid; 2-Aminobutyric acid; 4-Aminobutyric acid (Piperidinic
acid); 6-Aminocaproic acid; 2-Aminoheptanoic acid; 2Aminoisobutyric acid, 3-Aminoisobutyric acid; 2-Aminopimelic
acid; 2,4-Diaminobutyric acid; Desmosine; 2,2'Diaminopimelic acid; 2,3-Diaminopropionic acid; NEthylglycine; N-Ethylasparagine; Hydroxylysine; alloHydroxylysine; 3-Hydroxyproline; 4-Hydroxyproline;
Isodesmosine; allo-Isoleucine; N-Methylglycine (Sarcosine);
N-Methylisoleucine; N-Methylvaline; Norvaline; Norleucine;
and Ornithine.

Peptides are constructed by condensation of amino acids and/or smaller peptides. The amino group of one amino acid (or peptide) reacts with the carboxylic acid group of a second amino acid (or peptide) to form a peptide (-NHCO-) bond, releasing one molecule of water. Therefore, when an amino acid is incorporated into a peptide, it should,

technically speaking, be referred to as an amino acid residue. The core of that residue is the moiety which excludes the -NH and -CO linking functionalities which connect it to other residues. This moiety consists of one or more main chain atoms (see below) and the attached side chains.

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The main chain moiety of each amino acid consists of the -NH and -CO linking functionalities and a core main chain moiety. Usually the latter is a single carbon atom. However, the core main chain moiety may include additional carbon atoms, and may also include nitrogen, oxygen or sulfur atoms, which together form a single chain. In a preferred embodiment, the core main chain atoms consist solely of carbon atoms.

The side chains are attached to the core main chain atoms. For alpha amino acids, in which the side chain is attached to the alpha carbon, the C-1, C-2 and N-2 of each residue form the repeating unit of the main chain, and the word "side chain" refers to the C-3 and higher numbered carbon atoms and their substituents. It also includes H atoms attached to the main chain atoms.

Amino acids may be classified according to the number of carbon atoms which appear in the main chain between the carbonyl carbon and amino nitrogen atoms which participate in the peptide bonds. Among the 150 or so amino acids which occur in nature, alpha, beta, gamma and delta amino acids are known. These have 1-4 intermediary carbons. Only alpha amino acids occur in proteins. Proline is a special case of an alpha amino acid; its side chain also binds to the peptide bond nitrogen.

For beta and higher order amino acids, there is a choice as to which main chain core carbon a side chain other than H is attached to. The preferred attachment site is the C-2 (alpha) carbon, i.e., the one adjacent to the carboxyl carbon of the -CO linking functionality. It is also possible for more than one main chain atom to carry a side chain other than H. However, in a preferred embodiment, only one main chain core atom carries a side chain other than H.

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A main chain carbon atom may carry either one or two side chains; one is more common. A side chain may be attached to a main chain carbon atom by a single or a double bond; the former is more common.

A simple combinatorial peptide library is one whose members are peptides having three or more amino acids connected via peptide bonds.

The peptides may be linear, branched, or cyclic, and may covalently or noncovalently include nonpeptidyl moieties. The amino acids are not limited to the naturally occurring or to the genetically encoded amino acids.

A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues.

Cyclic Peptides

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Many naturally occurring peptides are cyclic. Cyclization is a common mechanism for stabilization of peptide conformation thereby achieving improved association of the peptide with its ligand and hence improved biological activity. Cyclization is usually achieved by intra-chain cystine formation, by formation of peptide bond between side chains or between N- and C- terminals. Cyclization was usually achieved by peptides in solution, but several publications have appeared that describe cyclization of peptides on beads.

A peptide library may be an oligopeptide library or a protein library.

30 Oligopeptides

Preferably, the oligopeptides are at least five, six, seven or eight amino acids in length. Preferably, they are composed of less than 50, more preferably less than 20 amino acids.

In the case of an oligopeptide library, all or just some of the residues may be variable. The oligopeptide may be unconstrained, or constrained to a particular conformation by, e.g., the participation of constant

cysteine residues in the formation of a constraining disulfide bond.

Proteins

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Proteins, like oligopeptides, are composed of a plurality of amino acids, but the term protein is usually reserved for longer peptides, which are able to fold into a stable conformation. A protein may be composed of two or more polypeptide chains, held together by covalent or noncovalent crosslinks. These may occur in a homooligomeric or a heterooligomeric state.

A peptide is considered a protein if it (1) is at least 50 amino acids long, or (2) has at least two stabilizing covalent crosslinks (e.g., disulfide bonds). Thus, conotoxins are considered proteins.

Usually, the proteins of a protein library will be characterizable as having both constant residues (the same for all proteins in the library) and variable residues (which vary from member to member). This is simply because, for a given range of variation at each position, the sequence space (simple diversity) grows exponentially with the number of residue positions, so at some point it becomes inconvenient for all residues of a peptide to be variable positions. Since proteins are usually larger than oligopeptides, it is more common for protein libraries than oligopeptide libraries to feature variable positions.

In the case of a protein library, it is desirable to focus the mutations at those sites which are tolerant of mutation. These may be determined by alanine scanning mutagenesis or by comparison of the protein sequence to that of homologous proteins of similar activity. It is also more likely that mutation of surface residues will directly affect binding. Surface residues may be determined by inspecting a 3D structure of the protein, or by labeling the surface and then ascertaining which residues have received labels. They may also be inferred by identifying regions of high hydrophilicity within the protein.

Because proteins are often altered at some sites but not others, protein libraries can be considered a special case of the biased peptide library.

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There are several reasons that one might screen a protein library instead of an oligopeptide library, including (1) a particular protein, mutated in the library, has the desired activity to some degree already, and (2) the oligopeptides are not expected to have a sufficiently high affinity or specificity since they do not have a stable conformation.

When the protein library is based on a parental protein which does not have the desired activity, the parental protein will usually be one which is of high stability (melting point >= 50 deg. C.) and/or possessed of hypervariable regions.

The variable domains of an antibody possess hypervariable regions and hence, in some embodiments, the protein library comprises members which comprise a mutant of VH or VL chain, or a mutant of an antigen-specific binding fragment of such a chain. VH and VL chains are usually each about 110 amino acid residues, and are held in proximity by a disulfide bond between the adjoing CL and CH1 regions to form a variable domain. Together, the VH, VL, CL and CH1 form an Fab fragment.

In human heavy chains, the hypervariable regions are at 31-35, 49-65, 98-111 and 84-88, but only the first three are involved in antigen binding. There is variation among VH and VL chains at residues outside the hypervariable regions, but to a much lesser degree.

A sequence is considered a mutant of a VH or VL chain if it is at least 80% identical to a naturally occurring VH or VL chain at all residues outside the hypervariable region.

In a preferred embodiment, such antibody library members comprise both at least one VH chain and at least one VL chain, at least one of which is a mutant chain, and which chains may be derived from the same or different antibodies. The VH and VL chains may be covalently joined by a suitable linker moiety, as in a "single chain antibody", or they may

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be noncovalently joined, as in a naturally occurring variable domain.

If the joining is noncovalent, and the library is displayed on cells or virus, then either the VH or the VL chain may be fused to the carrier surface/coat protein. The complementary chain may be co-expressed, or added exogenously to the library.

The members may further comprise some or all of an antibody constant heavy and/or constant light chain, or a mutant thereof.

Peptoid Library

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A peptoid is an analogue of a peptide in which one or more of the peptide bonds (-NH-CO-) are replaced by pseudopeptide bonds, which may be the same or different. It is not necessary that all of the peptide bonds be replaced, i.e., a peptoid may include one or more conventional amino acid residues, e.g., proline.

A peptide bond has two small divalent linker elements, -NH- and -CO-. Thus, a preferred class of psuedopeptide bonds are those which consist of two small divalent linker elements. Each may be chosen independently from the group consisting of amine (-NH-), substituted amine (-NR-), carbonyl (-CO-), thiocarbonyl (-CS-), methylene (-CH2-), monosubstituted methylene (-CHR-), disubstituted methylene (-CR1R2-), ether (-O-) and thioether (-S-). The more preferred pseudopeptide bonds include:

N-modified -NRCOCarba Ψ -CH₂-CH₂Depsi Ψ -CO-OHydroxyethylene Ψ -CHOH-CH₂Ketomethylene Ψ -CO-CH₂Methylene-Oxy -CH₂-OReduced -CH₂-NHThiomethylene -CH₂-SThiopeptide -CS-NHRetro-Inverso -CO-NH-

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A single peptoid molecule may include more than one kind of pseudopeptide bond.

For the purposes of introducing diversity into a peptoid library, one may vary (1) the side chains attached to the core main chain atoms of the monomers linked by the pseudopeptide bonds, and/or (2) the side chains (e.g., the -R of an -NRCO-) of the pseudopeptide bonds. Thus, in one embodiment, the monomeric units which are not amino acid residues are of the structure -NR1-CR2-CO-, where at least one of R1 and R2 are not hydrogen. If there is variability in the pseudopeptide bond, this is most conveniently done by using an -NRCO- or other pseudopeptide bond with an R group, and varying the R group. In this event, the R group will usually be any of the side chains characterizing the amino acids of peptides, as previously discussed.

If the R group of the pseudopeptide bond is not variable, it will usually be small, e.g., not more than 10 atoms (e.g., hydroxyl, amino, carboxyl, methyl, ethyl, propyl).

If the conjugation chemistries are compatible, a simple combinatorial library may include both peptides and peptoids.

Peptide Nucleic Acid Library

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A PNA oligomer is here defined as one comprising a plurality of units, at least one of which is a PNA monomer which comprises a side chain comprising a nucleobase. For nucleobases, see USP 6,077,835.

The classic PNA oligomer is composed of (2-aminoethyl)glycine units, with nucleobases attached by methylene carbonyl linkers. That is, it has the structure

$$H-(-HN-CH2-CH2-N(-CO-CH2-B)-CH2-CO-)n -OH$$

where the outer parenthesized substructure is the PNA monomer.

In this structure, the nucleobase B is separated from the backbone N by three bonds, and the points of attachment

of the side chains are separated by six bonds. The nucleobase may be any of the bases included in the nucleotides discussed in connection with oligonucleotide libraries. The bases of nucleotides A, G, T, C and U are preferred.

A PNA oligomer may further comprise one or more amino acid residues, especially glycine and proline.

One can readily envision related molecules in which (1) the -COCH2- linker is replaced by another linker, especially one composed of two small divalent linkers as defined previously, (2) a side chain is attached to one of the three main chain carbons not participating in the peptide bond (either instead or in addition to the side chain attached to the N of the classic PNA); and/or (3) the peptide bonds are replaced by pseudopeptide bonds as disclosed previously in the context of peptoids.

PNA oligomer libraries have been made; see e.g. Cook, 6,204,326.

20 Small Organic Compound Library

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The small organic compound library ("compound library", for short) is a combinatorial library whose members are suitable for use as drugs if, indeed, they have the ability to mediate a biological activity of the target protein.

Peptides have certain disadvantages as drugs. These include susceptibility to degradation by serum proteases, and difficulty in penetrating cell membranes. Preferably, all or most of the compounds of the compound library avoid, or at least do not suffer to the same degree, one or more of the pharmaceutical disadvantages of peptides.

In designing a compound library, it is helpful to bear in mind the methods of molecular modification typically used to obtain new drugs. Three basic kinds of modification may be identified: disjunction, in which a lead drug is simplified to identify its component pharmacophoric moieties; conjunction, in which two or more known pharmacophoric moieties, which may be the same or different, are associated, covalently or noncovalently, to form a new drug; and alteration, in which one moiety is replaced by

another which may be similar or different, but which is not in effect a disjunction or conjunction. The use of the terms "disjunction", "conjunction" and "alteration" is intended only to connote the structural relationship of the end product to the original leads, and not how the new drugs are actually synthesized, although it is possible that the two are the same.

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The process of disjunction is illustrated by the evolution of neostigmine (1931) and edrophonium (1952) from physostigmine (1925). Subsequent conjunction is illustrated by demecarium (1956) and ambenonium (1956).

Alterations may modify the size, polarity, or electron distribution of an original moiety. Alterations include ring closing or opening, formation of lower or higher homologues, introduction or saturation of double bonds, introduction of optically active centers, introduction, removal or replacement of bulky groups, isosteric or bioisosteric substitution, changes in the position or orientation of a group, introduction of alkylating groups, and introduction, removal or replacement of groups with a view toward inhibiting or promoting inductive (electrostatic) or conjugative (resonance) effects.

Thus, the substituents may include electron acceptors and/or electron donors. Typical electron donors (+I) include $-CH_3$, $-CH_2R$, $-CHR_2$, $-CR_3$ and $-COO^-$. Typical electron acceptors (-I) include $-NH_3+$, $-NR_3+$, $-NO_2$, -CN, -COOH, -COOR, -CHO, -COR, -COR, -F, -CI, -Br, -OH, -OR, -SH, -SR, $-CH=CH_2$, $-CR=CR_2$, and -C=CH.

The substituents may also include those which increase or decrease electronic density in conjugated systems. The former (+R) groups include -CH₃, -CR₃, -F, -C1, -Br, -I, -OH, -OR, -OCOR, -SH, -SR, -NH₂, -NR₂, and -NHCOR. The later (-R) groups include -NO₂, -CN, -CHC, -COR, -COOH, -COOR, -CONH₂, -SO₂R and -CF₃.

Synthetically speaking, the modifications may be achieved by a variety of unit processes, including nucleophilic and electrophilic substitution, reduction and oxidation, addition elimination, double bond cleavage, and cyclization.

For the purpose of constructing a library, a compound, or a family of compounds, having one or more pharmacological activities (which need not be related to the known or suspected activities of the target protein), may be disjoined into two or more known or potential pharmacophoric moieties. Analogues of each of these moieties may be identified, and mixtures of these analogues reacted so as to reassemble compounds which have some similarity to the original lead compound. It is not necessary that all members of the library possess moieties analogous to all of the moieties of the lead compound.

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The design of a library may be illustrated by the example of the benzodiazepines. Several benzodiazepine drugs, including chlordiazepoxide, diazepam and oxazepam, have been used as anti-anxiety drugs. Derivatives of benzodiazepines have widespread biological activities; derivatives have been reported to act not only as anxiolytics, but also as anticonvul sants; cholecystokinin (CCK) receptor subtype A or B, kappa opioid receptor, platelet activating factor, and HIV transactivator Tat antagonists, and GPIIbIIa, reverse transcriptase and ras farnesyltransferase inhibitors.

The benzodiazepine structure has been disjoined into a 2-aminobenzophenone, an amino acid, and an alkylating agent. See Bunin, et al., Proc. Nat. Acad. Sci. USA, 91:4708 (1994). Since only a few 2-aminobenzophenone derivatives are commercially available, it was later disjoined into 2-aminoarylstannane, an acid chloride, an amino acid, and an alkylating agent. Bunin, et al., Meth. Enzymol., 267:448 (1996). The arylstannane may be considered the core structure upon which the other moieties are substituted, or all four may be considered equals which are conjoined to make each library member.

A basic library synthesis plan and member structure is shown in Figure 1 of Fowlkes, et al_, U.S. Serial No. 08/740,671, incorporated by reference in its entirety. The acid chloride building block introduces variability at the R¹ site. The R² site is introduced by the amino acid, and the R³ site by the alkylating agent. The R⁴ site is inherent in

the arylstannane. Bunin, et al. generated a 1, 4-benzodiazepine library of 11,200 different derivatives prepared from 20 acid chlorides, 35 amino acids, and 16 alkylating agents. (No diversity was introduced at R4; this group was used to couple the molecule to a solid phase.) According to the Available Chemicals Directory (HDL Information Systems, San Leandro CA), over 300 acid chlorides, 80 Fmoc-protected amino acids and 800 alkylating agents were available for purchase (and more, of course, could be synthesized). The particular moieties used were chosen to maximize structural dispersion, while limiting the numbers to those conveniently synthesized in the wells of a microtiter plate. In choosing between structurally similar compounds, preference was given to the least substituted compound.

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The variable elements included both aliphatic and aromatic groups. Among the aliphatic groups, both acyclic and cyclic (mono- or poly-) structures, substituted or not, were tested. (While all of the acyclic groups were linear, it would have been feasible to introduce a branched aliphatic). The aromatic groups featured either single and multiple rings, fused or not, substituted or not, and with heteroatoms or not. The secondary substitutents included - NH₂, -OH, -OMe, -CN, -C1, -F, and -COOH. While not used, spacer moieties, such as -O-, -S-, -OO-, -CS-, -NH-, and -NR-, could have been incorporated.

Bunin et al. suggest that instead of using a 1, 4-benzodiazepine as a core structure, one may instead use a 1, 4-benzodiazepine-2, 5-dione structure.

As noted by Bunin et al., it is advantageous, although not necessary, to use a linkage strategy which leaves no trace of the linking functionality, as this permits construction of a more diverse library.

Other combinatorial nonoligomeric compound libraries known or suggested in the art have been based on carbamates, mercaptoacylated pyrrolidines, phenolic agents, aminimides, N-acylamino ethers (made from amino alcohols, aromatic hydroxy acids, and carboxylic acids), N-alkylamino ethers

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(made from aromatic hydroxy acids, amino alcohols and aldehydes) 1, 4-piperazines, and 1, 4-piperazine-6-ones.

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DeWitt, et al., Proc. Nat. Acad. Sci. (USA), 90:6909-13 (1993) describe the simultaneous but separate, synthesis of 40 discrete hydantoins and 40 discrete benzodiazepines. They carry out their synthesis on a solid support (inside a gas dispersion tube), in an array format, as opposed to other conventional simultaneous synthesis techniques (e.g., in a well, or on a pin). The hydantoins were synthesized by first simultaneously deprotecting and then treating each of five amino acid resins with each of eight isocyanates. The benzodiazepines were synthesized by treating each of five deprotected amino acid resins with each of eight 2-amino benzophenone imines.

Chen, et al., J. Am. Chem. Soc., 116:2661-62 (1994) described the preparation of a pilot (9 member) combinatorial library of formate esters. A polymer beadbound aldehyde preparation was "split" into three aliquots, each reacted with one of three different ylide reagents. The reaction products were combined, and then divided into three new aliquots, each of which was reacted with a different Michael donor. Compound identity was found to be determinable on a single bead basis by gas chromatography/mass spectroscopy analysis.

Holmes, USP 5,549,974 (1996) sets forth methodologies for the combinatorial synthesis of libraries of thiazolidinones and metathiazanones. These libraries are made by combination of amines, carbonyl compounds, and thiols under cyclization conditions.

Ellman, USP 5,545,568 (1996) describes combinatorial synthesis of benzodiazepines, prostaglandins, beta-turn mimetics, and glycerol-based compounds. See also Ellman, USP 5,288,514.

Summerton, USP 5,506,337 (1996) discloses methods of preparing a combinatorial library formed predominantly of morpholino subunit structures.

Heterocylic combinatorial libraries are reviewed generally in Nefzi, et al., Chem. Rev., 97:449-472 (1997).

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For pharmacological classes, see, e.g., Goth, Medical Pharmacology: Principles and Concepts (C.V. Mosby Co.: 8th ed. 1976); Korolkovas and Burckhalter, Essentials of Medicinal Chemistry (John Wiley & Sons, Inc.: 1976). For synthetic methods, see, e.g., Warren, Organic Synthesis: The Disconnection Approach (John Wiley & Sons, Ltd.: 1982); Fuson, Reactions of Organic Compounds (John Wiley & Sons: 1966); Payne and Payne, How to do an Organic Synthesis (Allyn and Bacon, Inc.: 1969); Greene, Protective Groups in Organic Synthesis (Wiley-Interscience). For selection of substituents, see e.g., Hansch and Leo, Substituent Constants for Correlation Analysis in Chemistry and Biology (John Wiley & Sons: 1979).

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The library is preferably synthesized so that the individual members remain identifiable so that, if a member is shown to be active, it is not necessary to analyze it. Several methods of identification have been proposed, including:

- (1) encoding, i.e., the attachment to each member of an identifier moiety which is more readily identified than the member proper. This has the disadvantage that the tag may itself influence the activity of the conjugate.
- (2) spatial addressing, e.g., each member is synthesized only at a particular coordinate on or in a matrix, or in a particular chamber. This might be, for example, the location of a particular pin, or a particular well on a microtiter plate, or inside a "tea bag".

The present invention is not limited to any particular form of identification.

However, it is possible to simply characterize those members of the library which are found to be active, based on the characteristic spectroscopic indicia of the various building blocks.

Solid phase synthesis permits greater control over which derivatives are formed. However, the solid phase could interfere with activity. To overcome this problem,

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some or all of the molecules of each member could be liberated, after synthesis but before screening.

Examples of candidate simple libraries which might be evaluated include derivatives of the following:

Cyclic Compounds Containing One Hetero Atom Heteronitrogen

pyrroles

pentasubstituted pyrroles

pyrrolidines

pyrrolines

prolines

indoles

beta-carbolines

pyridines

15 dihydropyridines

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1,4-dihydropyridines

pyrido [2, 3-d] pyrimidines

tetrahydro-3H-imidazo[4,5-c] pyridines

Isoquinolines

tetrahydroisoguinolines

quinolones

beta-lactams

azabicyclo[4.3.0] nonen-8-One amino acid

Heterooxygen

furans

tetrahydrofurans

2,5-disubstituted tetrahydrofurans

pyrans

hydroxypyranones

tetrahydroxypyranones

gamma-butyrolactones

Heterosulfur

sulfolenes

Cyclic Compounds with Two or More Hetero atoms

Multiple heteronitrogens

imidazoles

pyrazoles

piperazines

diketopiperazines

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arylpiperazines benzylpiperazines

benzodiazepines

1,4-benzodiazepine-2,5-diones

hydantoins

5-alkoxyhydantoins

dihydropyrimidines

1,3-disubstituted-5,6-dihydopyrimidine-2,4-

10 diones

cyclic ureas

cyclic thioureas

quinazolines

chiral 3-substituted-quinazoline-2,4-

15 diones

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triazoles

1,2,3-triazoles

purines

Heteronitrogen and Heterooxygen

dikelomorpholines

isoxazoles

isoxazolines

Heteronitrogen and Heterosulfur

thiazolidines

25 N-axylthiazolidines

dihydrothiazoles

2-methylene-2,3-dihydrothiazates

2-aminothiazoles

thiophenes

3-amino thiophenes

4-thiazolidinones

4-melathiazanones

benzisothiazolones

For details on synthesis of libraries, see Nefzi, et al., Chem. Rev., 97:449-72 (1997), and references cited therein.

Pharmaceutical Methods and Preparations

The preferred animal subject of the present invention is a mammal. By the term "mammal" is meant an individual belonging to the class Mammalia. The invention is particularly useful in the treatment of human subjects, although it is intended for veterinary and nutritional uses as well. Preferred nonhuman subjects are of the orders Primata (e.g., apes and monkeys), Artiodactyla or Perissodactyla (e.g., cows, pigs, sheep, horses, goats), Carnivora (e.g., cats, dogs), Rodenta (e.g., rats, mice, guinea pigs, hamsters), Lagomorpha (e.g., rabbits) or other pet, farm or laboratory mammals.

The term "protection", as used herein, is intended to include "prevention," "suppression" and "treatment."

"Prevention", strictly speaking, involves administration of the pharmaceutical prior to the induction of the disease (or other adverse clinical condition). "Suppression" involves administration of the composition prior to the clinical appearance of the disease. "Treatment" involves administration of the protective composition after the appearance of the disease.

It will be understood that in human and veterinary medicine, it is not always possible to distinguish between "preventing" and "suppressing" since the ultimate inductive event or events may be unknown, latent, or the patient is not ascertained until well after the occurrence of the event or events. Therefore, unless qualified, the term "prevention" will be understood to refer to both prevention in the strict sense, and to suppression.

The preventative or prophylactic use of a pharmaceutical usually involves identifying subjects who are at higher risk than the general population of contracting the disease, and administering the pharmaceutical to them in advance of the clinical appearance of the disease. The effectiveness of such use is measured by comparing the subsequent incidence or severity of the disease, or of particular symptoms of the disease, in the treated subjects against that in untreated subjects of the same high risk group.

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While high risk factors vary from disease to disease, in general, these include (1) prior occurrence of the disease in one or more members of the same family, or, in the case of a contagious disease, in individuals with whom the subject has come into potentially contagious contact at a time when the earlier victim was likely to be contagious, (2) a prior occurrence of the disease in the subject, (3) prior occurrence of a related disease, or a condition known to increase the likelihood of the disease, in the subject; (4) appearance of a suspicious level of a marker of the disease, or a related disease or condition; (5) a subject who is immunologically compromised, e.g., by radiation treatment, HIV infection, drug use,, etc., or (6) membership in a particular group (e.g., a particular age, sex, race, ethnic group, etc.) which has been epidemiologically associated with that disease.

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In some cases, it may be desirable to provide prophylaxis for the general population, and not just a high risk group. This is most likely to be the case when essentially all are at risk of contracting the disease, the effects of the disease are serious, the therapeutic index of the prophylactic agent is high, and the cost of the agent is low.

A prophylaxis or treatment may be curative, that is, directed at the underlying cause of a disease, or ameliorative, that is, directed at the symptoms of the disease, especially those which reduce the quality of life.

It should also be understood that to be useful, the protection provided need not be absolute, provided that it is sufficient to carry clinical value. An agent which provides protection to a lesser degree than do competitive agents may still be of value if the other agents are ineffective for a particular individual, if it can be used in combination with other agents to enhance the level of protection, or if it is safer than competitive agents. It is desirable that there be a statistically significant (p=0.05 or less) improvement in the treated subject relative to an appropriate untreated control, and it is desirable that this improvement be at least 10%, more preferably at least 25%,

still more preferably at least 50%, even more preferably at least 100%, in some indicia of the incidence or severity of the disease or of at least one symptom of the disease.

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At least one of the drugs of the present invention may be administered, by any means that achieve their intended purpose, to protect a subject against a disease or other adverse condition. The form of administration may be systemic or topical. For example, administration of such a composition may be by various parenteral routes such as subcutaneous, intravenous, intradermal, intramuscular, intraperitoneal, intranasal, transdermal, or buccal routes. Alternatively, or concurrently, administration may be by the oral route. Parenteral administration can be by bolus injection or by gradual perfusion over time.

A typical regimen comprises administration of an effective amount of the drug, administered over a period ranging from a single dose, to dosing over a period of hours, days, weeks, months, or years.

It is understood that the suitable dosage of a drug of the present invention will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired. However, the most preferred dosage can be tailored to the individual subject, as is understood and determinable by one of skill in the art, without undue experimentation. This will typically involve adjustment of a standard dose, e.g., reduction of the dose if the patient has a low body weight.

Prior to use in humans, a drug will first be evaluated for safety and efficacy in laboratory animals. In human clinical studies, one would begin with a dose expected to be safe in humans, based on the preclinical data for the drug in question, and on customary doses for analogous drugs (if any). If this dose is effective, the dosage may be decreased, to determine the minimum effective dose, if desired. If this dose is ineffective, it will be cautiously increased, with the patients monitored for signs of side effects. See, e.g., Berkow et al, eds., The Merck Manual, 15th edition, Merck and Co., Rahway, N.J., 1987; Goodman et

al., eds., Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th edition, Pergamon Press, Inc., Elmsford, N.Y., (1990); Avery's Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987), Ebadi, Pharmacology, Little, Brown and Co., Boston, (1985), which references and references cited therein, are entirely incorporated herein by reference.

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The total dose required for each treatment may be administered by multiple doses or in a single dose. The protein may be administered alone or in conjunction with other therapeutics directed to the disease or directed to other symptoms thereof.

Typical pharmaceutical doses, for adult humans, are in the range of 1 ng to 10g per day, more often 1 mg to 1g per day.

The appropriate dosage form will depend on the disease, the pharmaceutical, and the mode of administration; possibilities include tablets, capsules, lozenges, dental pastes, suppositories, inhalants, solutions, ointments and parenteral depots. See, e.g., Berker, supra, Goodman, supra, Avery, supra and Ebadi, supra, which are entirely incorporated herein by reference, including all references cited therein.

In the case of peptide drugs, the drug may be administered in the form of an expression vector comprising a nucleic acid encoding the peptide; such a vector, after incorporation into the genetic complement of a cell of the patient, directs synthesis of the peptide. Suitable vectors include genetically engineered poxviruses (vaccinia), adenoviruses, adeno-associated viruses, herpesviruses and lentiviruses which are or have been rendered nonpathogenic.

In addition to at least one drug as described herein, a pharmaceutical composition may contain suitable pharmaceutically acceptable carriers, such as excipients, carriers and/or auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. See, e.g., Berker, supra, Goodman, supra, Avery, supra and Ebadi, supra, which are entirely

incorporated herein by reference, included all references cited therein.

Assay Compositions and Methods

Target Organism

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The invention contemplates that it may be appropriate to ascertain or to mediate the biological activity of a substance of this invention in a target organism.

The target organism may be a plant, animal, or microorganism.

In the case of a plant, it may be an economic plant, in which case the drug may be intended to increase the disease, weather or pest resistance, alter the growth characteristics, or otherwise improve the useful characteristics or mute undesirable characteristics of the plant. Or it may be a weed, in which case the drug may be intended to kill or otherwise inhibit the growth of the plant, or to alter its characteristics to convert it from a weed to an economic plant. The plant may be a tree, shrub, crop, grass, etc. The plant may be an algae (which are in some cases also microorganisms), or a vascular plant, especially gymnosperms (particularly conifers) and angiosperms. Angiosperms may be monocots or dicots. plants of greatest interest are rice, wheat, corn, alfalfa, soybeans, potatoes, peanuts, tomatoes, melons, apples, pears, plums, pineapples, fir, spruce, pine, cedar, and oak.

If the target organism is a microorganism, it may be algae, bacteria, fungi, or a virus (although the biological activity of a virus must be determined in a virus-infected cell). The microorganism may be human or other animal or plant pathogen, or it may be nonpathogenic. It may be a soil or water organism, or one which normally lives inside other living things.

If the target organism is an animal, it may be a vertebrate or a nonvertebrate animal. Nonvertebrate animals are chiefly of interest when they act as pathogens or parasites, and the drugs are intended to act as biocidic or biostatic agents. Nonvertebrate animals of interest include worms, mollusks, and arthropods.

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The target organism may also be a vertebrate animal, i.e., a mammal, bird, reptile, fish or amphibian. Among mammals, the target animal preferably belongs to the order Primata (humans, apes and monkeys), Artiodactyla (e.g., cows, pigs, sheep, goats, horses), Rodenta (e.g., mice, rats) Lagomorpha (e.g., rabbits, hares), or Carnivora (e.g., cats, dogs). Among birds, the target animals are preferably of the orders Anseriformes (e.g., ducks, geese, swans) or Galliformes (e.g., quails, grouse, pheasants, turkeys and chickens). Among fish, the target animal is preferably of the order Clupeiformes (e.g., sardines, shad, anchovies, whitefish, salmon).

Target Tissues

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The term "target tissue" refers to any whole animal, physiological system, whole organ, part of organ, miscellaneous tissue, cell, or cell component (e.g., the cell membrane) of a target animal in which biological activity may be measured.

Routinely in mammals one would choose to compare and contrast the biological impact on virtually any and all tissues which express the subject receptor protein. The main tissues to use are: brain, heart, lung, kidney, liver, pancreas, skin, intestines, adipose, stomach, skeletal muscle, adrenal glands, breast, prostate, vasculature, retina, cornea, thyroid gland, parathyroid glands, thymus, bone marrow, bone, etc.

Another classification would be by cell type: B cells, T cells, macrophages, neutrophils, eosinophils, mast cells, platelets, megakaryocytes, erythrocytes, bone marrow stomal cells, fibroblasts, neurons, astrocytes, neuroglia, microglia, epithelial cells (from any organ, e.g. skin, breast, prostate, lung, intestines etc), cardiac muscle cells, smooth muscle cells, striated muscle cells, osteoblasts, osteocytes, chondroblasts, chondrocytes, keratinocytes, melanocytes, etc.

Of course, in the case of a unicellular organism, there is no distinction between the "target organism" and the "target tissue".

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Screening Assays

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Assays intended to determine the binding or the biological activity of a substance are called preliminary screening assays.

Screening assays will typically be either in vitro (cell-free) assays (for binding to an immobilized receptor) or cell-based assays (for alterations in the phenotype of the cell). They will not involve screening of whole multicellular organisms, or isolated organs. The comments on diagnostic biological assays apply mutatis mutandis to screening cell-based assays.

<u>In Vitro vs. In Vivo Assays</u>

The term in vivo is descriptive of an event, such as binding or enzymatic action, which occurs within a living organism. The organism in question may, however, be genetically modified. The term in vitro refers to an event which occurs outside a living organism. Parts of an organism (e.g., a membrane, or an isolated biochemical) are used, together with artificial substrates and/or conditions. For the purpose of the present invention, the term in vitro excludes events occurring inside or on an intact cell, whether of a unicellular or multicellular organism.

In vivo assays include both cell-based assays, and organismic assays. The cell-based assays include both assays on unicellular organisms, and assays on isolated cells or cell cultures derived from multicellular organisms. The cell cultures may be mixed, provided that they are not organized into tissues or organs. The term organismic assay refers to assays on whole multicellular organisms, and assays on isolated organs or tissues of such organisms.

In vitro Diagnostic Methods and Reagents

The in vitro assays of the present invention may be applied to any suitable analyte-containing sample, and may be qualitative or quantitative in nature.

Sample

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The sample will normally be a biological fluid, such as blood, urine, lymph, semen, milk, or cerebrospinal fluid, or a fraction or derivative thereof, or a biological tissue, in the form of, e.g., a tissue section or homogenate. However, the sample conceivably could be (or derived from) a food or beverage, a pharmaceutical or diagnostic composition, soil, or surface or ground water. If a biological fluid or tissue, it may be taken from a human or other mammal, vertebrate or animal, or from a plant. The preferred sample is blood, or a fraction or derivative thereof.

Binding and Reaction Assays

The assay may be a binding assay, in which one step involves the binding of a diagnostic reagent to the analyte, or a reaction assay, which involves the reaction of a reagent with the analyte. The reagents used in a binding assay may be classified as to the nature of their interaction with analyte: (1) analyte analogues, or (2) analyte binding molecules (ABM). They may be labeled or insolubilized.

In a reaction assay, the assay may look for a direct reaction between the analyte and a reagent which is reactive with the analyte, or if the analyte is an enzyme or enzyme inhibitor, for a reaction catalyzed or inhibited by the analyte. The reagent may be a reactant, a catalyst, or an inhibitor for the reaction.

An assay may involve a cascade of steps in which the product of one step acts as the target for the next step. These steps may be binding steps, reaction steps, or a combination thereof.

Signal Producing System (SPS)

In order to detect the presence, or measure the amount, of an analyte, the assay must provide for a signal producing system (SPS) in which there is a detectable difference in the signal produced, depending on whether the analyte is present or absent (or, in a quantitative assay, on the

amount of the analyte). The detectable signal may be one which is visually detectable, or one detectable only with instruments. Possible signals include production of colored or luminescent products, alteration of the characteristics (including amplitude or polarization) of absorption or emission of radiation by an assay component or product, and precipitation or agglutination of a component or product. The term "signal" is intended to include the discontinuance of an existing signal, or a change in the rate of change of an observable parameter, rather than a change in its absolute value. The signal may be monitored manually or automatically.

In a reaction assay, the signal is often a product of the reaction. In a binding assay, it is normally provided by a label borne by a labeled reagent.

Labels

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The component of the signal producing system which is most intimately associated with the diagnostic reagent is called the "label". A label may be, e.g., a radioisotope, a fluorophore, an enzyme, a co-enzyme, an enzyme substrate, an electron-dense compound, an agglutinable particle.

The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography. Isotopes which are particularly useful for the purpose of the present invention include ³H, ¹²⁵I, ¹³¹I, ³⁵S, ¹⁴C, ³²P and ³³P. ¹²⁵I is preferred for antibody labeling.

The label may also be a fluorophore. When the fluorescently labeled reagent is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycocrythrin, phycocyanin, allophycocyanin, ophthaldehyde and fluorescamine.

Alternatively, fluorescence-emitting metals such as ¹²⁵Eu, or others of the lanthanide series, may be incorporated into a diagnostic reagent using such metal

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chelating groups as diethylenetriaminepentaacetic acid (DTPA) of ethylenediamine-tetraacetic acid (EDTA).

The label may also be a chemiluminescent compound. The presence of the chemiluminescently labeled reagent is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of particularly useful chemiluminescent labeling compounds are luminol, isolumino, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used for labeling. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Enzyme labels, such as horseradish peroxidase and alkaline phosphatase, are preferred. When an enzyme label is used, the signal producing system must also include a substrate for the enzyme. If the enzymatic reaction product is not itself detectable, the SPS will include one or more additional reactants so that a detectable product appears.

An enzyme analyte may act as its own label if an enzyme inhibitor is used as a diagnostic reagent.

Binding Assay Formats

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Binding assays may be divided into two basic types, heterogeneous and homogeneous. In heterogeneous assays, the interaction between the affinity molecule and the analyte does not affect the label, hence, to determine the amount or presence of analyte, bound label must be separated from free label. In homogeneous assays, the interaction does affect the activity of the label, and therefore analyte levels can be deduced without the need for a separation step.

In one embodiment, the ABM is insolubilized by coupling it to a macromolecular support, and analyte in the sample is allowed to compete with a known quantity of a labeled or specifically labelable analyte analogue. The "analyte

analogue" is a molecule capable of competing with analyte for binding to the ABM, and the term is intended to include analyte itself. It may be labeled already, or it may be labeled subsequently by specifically binding the label to a moiety differentiating the analyte analogue from analyte. The solid and liquid phases are separated, and the labeled analyte analogue in one phase is quantified. The higher the level of analyte analogue in the solid phase, i.e., sticking to the ABM, the lower the level of analyte in the sample.

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In a "sandwich assay", both an insolubilized ABM, and a labeled ABM are employed. The analyte is captured by the insolubilized ABM and is tagged by the labeled ABM, forming a ternary complex. The reagents may be added to the sample in either order, or simultaneously. The ABMs may be the same or different. The amount of labeled ABM in the ternary complex is directly proportional to the amount of analyte in the sample.

The two embodiments described above are both heterogeneous assays. However, homogeneous assays are conceivable. The key is that the label be affected by whether or not the complex is formed. Conjugation Methods

A label may be conjugated, directly or indirectly (e.g., through a labeled anti-ABM antibody), covalently (e.g., with SPDP) or noncovalently, to the ABM, to produce a diagnostic reagent. Similarly, the ABM may be conjugated to a solid phase support to form a solid phase ("capture") diagnostic reagent.

Suitable supports include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention.

The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to its target. Thus the support configuration may be spherical, as in a bead, or

cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc.

5 Biological Assays

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A biological assay measures or detects a biological response of a biological entity to a substance.

The biological entity may be a whole organism, an isolated organ or tissue, freshly isolated cells, an immortalized cell line, or a subcellular component (such as a membrane; this term should not be construed as including an isolated receptor). The entity may be, or may be derived from, an organism which occurs in nature, or which is modified in some way. Modifications may be genetic (including radiation and chemical mutants, and genetic engineering) or somatic (e.g., surgical, chemical, etc.). In the case of a multicellular entity, the modifications may affect some or all cells. The entity need not be the target organism, or a derivative thereof, if there is a reasonable correlation between bioassay activity in the assay entity and biological activity in the target organism.

The entity is placed in a particular environment, which may be more or less natural. For example, a culture medium may, but need not, contain serum or serum substitutes, and it may, but need not, include a support matrix of some kind, it may be still, or agitated. It may contain particular biological or chemical agents, or have particular physical parameters (e.g., temperature), that are intended to nourish or challenge the biological entity.

There must also be a detectable biological marker for the response. At the cellular level, the most common markers are cell survival and proliferation, cell behavior (clustering, motility), cell morphology (shape, color), and biochemical activity (overall DNA synthesis, overall protein synthesis, and specific metabolic activities, such as utilization of particular nutrients, e.g., consumption of oxygen, production of CO₂, production of organic acids, uptake or discharge of ions).

The direct signal produced by the biological marker may be transformed by a signal producing system into a different signal which is more observable, for example, a fluorescent or colorimetric signal.

The entity, environment, marker and signal producing system are chosen to achieve a clinically acceptable level of sensitivity, specificity and accuracy.

In some cases, the goal will be to identify substances which mediate the biological activity of a natural biological entity, and the assay is carried out directly with that entity. In other cases, the biological entity is used simply as a model of some more complex (or otherwise inconvenient to work with) biological entity. In that event, the model biological entity is used because activity in the model system is considered more predictive of activity in the ultimate natural biological entity than is simple binding activity in an in vitro system. The model entity is used instead of the ultimate entity because the former is more expensive or slower to work with, or because ethical considerations forbid working with the ultimate entity yet.

The model entity may be naturally occurring, if the model entity usefully models the ultimate entity under some conditions. Or it may be non-naturally occurring, with modifications that increase its resemblance to the ultimate entity.

Transgenic animals, such as transgenic mice, rats, and rabbits, have been found useful as model systems.

In cell-based model assays, where the biological activity is mediated by binding to a receptor (target protein), the receptor may be functionally connected to a signal (biological marker) producing system, which may be endogenous or exogenous to the cell.

There are a number of techniques of doing this.

"Zero-Hybrid" Systems

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In these systems, the binding of a peptide to the target protein results in a screenable or selectable phenotypic change, without resort to fusing the target

protein (or a ligand binding moiety thereof) to an endogenous protein. It may be that the target protein is endogenous to the host cell, or is substantially identical to an endogenous receptor so that it can take advantage of the latter's native signal transduction pathway. Or sufficient elements of the signal transduction pathway normally associated with the target protein may be engineered into the cell so that the cell signals binding to the target protein.

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"One-Hybrid" Systems

In these systems, a chimera receptor, a hybrid of the target protein and an endogenous receptor, is used. The chimeric receptor has the ligand binding characteristics of the target protein and the signal transduction characteristics of the endogenous receptor. Thus, the normal signal transduction pathway of the endogenous receptor is subverted.

Preferably, the endogenous receptor is inactivated, or the conditions of the assay avoid activation of the endogenous receptor, to improve the signal-to-noise ratio.

See Fowlkes USP 5,789,184 for a yeast system.

Another type of "one-hybrid" system combines a peptide: DNA-binding domain fusion with an unfused target receptor that possesses an activation domain.

"Two-Hybrid" System

In a preferred embodiment, the cell-based assay is a two hybrid system. This term implies that the ligand is incorporated into a first hybrid protein, and the receptor into a second hybrid protein. The first hybrid also comprises component A of a signal generating system, and the second hybrid comprises component B of that system.

Components A and B, by themselves, are insufficient to generate a signal. However, if the ligand binds the receptor, components A and B are brought into sufficiently close proximity so that they can cooperate to generate a signal.

Components A and B may naturally occur, or be substantially identical to moieties which naturally occur, as components of a single naturally occurring biomolecule, or they may naturally occur, or be substantially identical to moieties which naturally occur, as separate naturally occurring biomolecules which interact in nature.

Two-Hybrid System: Transcription Factor Type

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In a preferred "two-hybrid" embodiment, one member of a peptide ligand:receptor binding pair is expressed as a fusion to a DNA-binding domain (DBD) from a transcription factor (this fusion protein is called the "bait"), and the other is expressed as a fusion to a transactivation domain (TAD) (this fusion protein is called the "fish", the "prey", or the "catch"). The transactivation domain should be complementary to the DNA-binding domain, i.e., it should interact with the latter so as to activate transcription of a specially designed reporter gene that carries a binding site for the DNA-binding domain. Naturally, the two fusion proteins must likewise be complementary.

This complementarity may be achieved by use of the complementary and separable DNA-binding and transcriptional activator domains of a single transcriptional activator protein, or one may use complementary domains derived from different proteins. The domains may be identical to the native domains, or mutants thereof. The assay members may be fused directly to the DBD or TAD, or fused through an intermediated linker.

The target DNA operator may be the native operator sequence, or a mutant operator. Mutations in the operator may be coordinated with mutations in the DBD and the TAD. An example of a suitable transcription activation system is one comprising the DNA-binding domain from the bacterial repressor LexA and the activation domain from the yeast transcription factor Gal4, with the reporter gene operably linked to the LexA operator.

It is not necessary to employ the intact target receptor; just the ligand-binding moiety is sufficient.

The two fusion proteins may be expressed from the same or different vectors. Likewise, the activatable reporter gene may be expressed from the same vector as either fusion protein (or both proteins), or from a third vector.

Potential DNA-binding domains include Gal4, LexA, and mutant domains substantially identical to the above.

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Potential activation domains include E. coli B42, Gal4 activation domain II, and HSV VP16, and mutant domains substantially identical to the above.

Potential operators include the native operators for the desired activation domain, and mutant domains substantially identical to the native operator.

The fusion proteins may comprise nuclear localization signals.

The assay system will include a signal producing system, too. The first element of this system is a reporter gene operably linked to an operator responsive to the DBD and TAD of choice. The expression of this reporter gene will result, directly or indirectly, in a selectable or screenable phenotype (the signal). The signal producing system may include, besides the reporter gene, additional genetic or biochemical elements which cooperate in the production of the signal. Such an element could be, for example, a selective agent in the cell growth medium. There may be more than one signal producing system, and the system may include more than one reporter gene.

The sensitivity of the system may be adjusted by, e.g., use of competitive inhibitors of any step in the activation or signal production process, increasing or decreasing the number of operators, using a stronger or weaker DBD or TAD, etc.

When the signal is the death or survival of the cell in question, or proliferation or monproliferation of the cell in question, the assay is said to be a selection. When the signal merely results in a detectable phenotype by which the signaling cell may be differentiated from the same cell in a nonsignaling state (either way being a living cell), the assay is a screen. However, the term "screening assay" may be used in a broader sense to include a selection. When the

narrower sense is intended, we will use the term "nonselective screen".

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Various screening and selection systems are discussed in Ladner, USP 5,198,346.

Screening and selection may be for or against the peptide: target protein or compound:target protein interaction.

Preferred assay cells are microbial (bacterial, yeast, algal, protozooal), invertebrate, vertebrate (esp. mammalian, particularly human). The best developed two-hybrid assays are yeast and mammalian systems.

Normally, two hybrid assays are used to determine whether a protein X and a protein Y interact, by virtue of their ability to reconstitute the interaction of the DBD and the TAD. However, augmented two-hybrid assays have been used to detect interactions that depend on a third, non-protein ligand.

For more guidance on two-hybrid assays, see Brent and Finley, Jr., Ann. Rev. Genet., 31:663-704 (1997); Fremont-Racine, et al., Nature Genetics, 277-281 (16 July 1997); Allen, et al., TIBS, 511-16 (Dec. 1995); LeCrenier, et al., BioEssays, 20:1-6 (1998); Xu, et al., Proc. Nat. Acad. sci. (USA), 94:12473-8 (Nov. 1992); Esotak, et al., Mol. Cell. Biol., 15:5820-9 (1995); Yang, et al., Nucleic Acids Res., 23:1152-6 (1995); Bendixen, et al., Nucleic Acids Res., 22:1778-9 (1994); Fuller, et al., BioTechniques, 25:85-92 (July 1998); Cohen, et al., PNAS (USA) 95:14272-7 (1998); Kolonin and Finley, Jr., PNAS (USA) 95:14266-71 (1998). See also Vasavada, et al., PNAS (USA), 88:10686-90 (1991) (contingent replication assay), and Rehrauer, et al., J. Biol. Chem., 271:23865-73 91996) (LexA repressor cleavage assay).

Two-Hybrid Systems: reporter Enzyme type

In another embodiment, the components A and B
reconstitute an enzyme which is not a transcription factor.

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As in the last example, the effect of the reconstitution of the enzyme is a phenotypic change which may be a screenable change, a selectable change, or both.

In vivo Diagnostic Uses

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Radio-labeled ABM may be administered to the human or animal subject. Administration is typically by injection, e.g., intravenous or arterial or other means of administration in a quantity sufficient to permit subsequent dynamic and/or static imaging using suitable radio-detecting devices. The dosage is the smallest amount capable of providing a diagnostically effective image, and may be determined by means conventional in the art, using known radio-imaging agents as a guide.

Typically, the imaging is carried out on the whole body of the subject, or on that portion of the body or organ relevant to the condition or disease under study. The amount of radio-labeled ABM accumulated at a given point in time in relevant target organs can then be quantified.

A particularly suitable radio-detecting device is a scintillation camera, such as a gamma camera. A scintillation camera is a stationary device that can be used to image distribution of radio-labeled ABM. The detection device in the camera senses the radioactive decay, the distribution of which can be recorded. Data produced by the imaging system can be digitized. The digitized information can be analyzed over time discontinuously or continuously. The digitized data can be processed to produce images, called frames, of the pattern of uptake of the radio-labeled ABM in the target organ at a discrete point in time. most continuous (dynamic) studies, quantitative data is obtained by observing changes in distributions of radioactive decay in target organs over time. In other words, a time-activity analysis of the data will illustrate uptake through clearance of the radio-labeled binding protein by the target organs with time.

Various factors should be taken into consideration in selecting an appropriate radioisotope. The radioisotope must be selected with a view to obtaining good quality

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resolution upon imaging, should be safe for diagnostic use in humans and animals, and should preferably have a short physical half-life so as to decrease the amount of radiation received by the body. The radioisotope used should preferably be pharmacologically inert, and, in the quantities administered, should not have any substantial physiological effect.

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The ABM may be radio-labeled with different isotopes of iodine, for example ¹²³I, ¹²⁵I, or ¹³¹I (see for example, U.S. Patent 4,609,725). The extent of radio-labeling must, however be monitored, since it will affect the calculations made based on the imaging results (i.e. a diiodinated ABM will result in twice the radiation count of a similar monoiodinated ABM over the same time frame).

In applications to human subjects, it may be desirable to use radioisotopes other than ¹²⁵I for labeling in order to decrease the total dosimetry exposure of the human body and to optimize the detectability of the labeled molecule (though this radioisotope can be used if circumstances require). Ready availability for clinical use is also a factor. Accordingly, for human applications, preferred radio-labels are for example, ^{99m}Tc, ⁶⁷Ga, ⁶⁸Ga, ⁹⁰Y, ¹¹¹In, ^{113m}In, ¹²³I, ¹⁸⁶Re, ¹⁸⁸Re or ²¹¹At.

The radio-labeled ABM may be prepared by various methods. These include radio-halogenation by the chloramine - T method or the lactoperoxidase method and subsequent purification by HPLC (high pressure liquid chromatography), for example as described by J. Gutkowska et al in "Endocrinology and Metabolism Clinics of America: (1987) 16 (1):183. Other known methods of radio-labeling can be used, such as IODOBEADS™.

There are a number of different methods of delivering the radio-labeled ABM to the end-user. It may be administered by any means that enables the active agent to reach the agent's site of action in the body of a mammal. Because proteins are subject to being digested when administered orally, parenteral administration, i.e., intravenous, subcutaneous, intramuscular, would ordinarily

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EXAMPLES

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We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat and has been documented to lead to diabetes in C57BL/6J mice (Surwit at al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets. At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. For further analysis, RNA was extracted from the gastrocnemius muscles at each time point and used in DNA microarray analyses.

15 Animal Models.

Obesity and subsequent hyperinsulinemia and hyperglycemia were induced by feeding a group of 3 week old mice (50 C57BL/6 males) a high-fat diet (Bio-Serve, Frenchtown, NJ, #F1850 High Carbohydrate-High Fat; 56% of calories from fat, 16% from protein and 27% from carbohydrates). Another group of 3 week old mice (20 C57B1/6 males) were fed the normal control diet (PMI Nutrition International Inc., Brentwood, MO, Prolab RMH3000; 14% of calories from fat, 16% from protein and 60% from carbohydrates). The mice were placed onto the respective diets immediately following weaning. Animal weights were determined weekly. Fasting blood-glucose and plasma insulin measurements were determined after 2, 4, 8 and 16 weeks on the respective diets.

The day after obtaining body weight measurements at the indicated time points, mice were fasted 8 hours and blood glucose concentrations were measured via tail blood samples using a One Touch Glucometer (Lifescan). For insulin measurements, blood was collected into heparinized tubes, plasma obtained by centrifugation and insulin concentrations determined using an Ultra-Sensitive Rat Insulin ELISA kit (ALPCO) as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for species difference in cross-

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reactivity with the antibody (bottom panel). Results reflect mean \pm SE of 50 mice on the HF diet and 20 mice on the Std diet.

Normal weight, normal fasting blood glucose and normal fasting plasma insulin levels are defined as the respective mean values of the animals fed the control diet.

Two of the "most typical" animals were selected for each group (Control, hyperinsulinemic and Diabetic) at each time point (2,4,8, and 16 weeks after commencement of diet) for sacrifice. The selected mice were sacrificed and muscle tissue obtained and immediately processed for RNA isolation.

Fasting Blood Glucose Levels.

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Blood glucose levels was measured from a drop of blood taken from the tip of the tail of fasted (8 hr) mice using a Lifescan Genuine One Touch glucometer. All measurements occurred between 2:00 pm and 5:00 pm.

Plasma insulin measurements.

Blood was collected from the tail of fasted (8 hr) mice into a heparinized capillary tube and stored on ice. All collections occurred between 2:00 pm and 5:00 pm. Plasma was separated from red blood cells by centrifugation for 10 minutes at 8000 x g and then stored at -20°C. Insulin concentrations were determined using the Rat Insulin ELISA kit and rat insulin standards (ALPCO) essentially as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for the species difference in cross-reactivity with the antibody.

RNA isolation.

Total RNA was isolated from muscle (skeletal muscle, specifically, gastrocnemius) of two mice at each time point during the progression of HF diet-induced type 2 diabetes, as well as age-matched controls on the Std diet, using the RNA STAT-60 Total RNA/mRNA Isolation Reagent according to the manufacturer's instructions (Tel-Test, Friendswood, TX).

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Sample Quantification and Quality Assessment

Total RNA was quantified and assessed for quality on a Bioanalyzer RNA 6000 Nano chip (Agilent). Each chip contained an interconnected set of gel-filled channels that allowed for molecular sieving of mucleic acids. Pinelectrodes in the chip were used to create electrokinetic forces capable of driving molecules through these microchannels to perform electrophoretic separations. Ribosomal peaks were measured by fluorescence signal and displayed in an electropherogram. A successful total RNA sample featured 2 distinct ribosomal peaks (18S and 28S rRNA).

Biotinylated cRNA Hybridization Target.

Total RNA was prepared for use as a hybridization target as described in the manufacturer's instructions for CodeLink Expression Bioarrays(TM) (Amersham Biosciences). The CodeLink Expression Bioarrays utilize nucleic acid hybridization of a biotin-labeled complementary RNA(cRNA) target with DNA oligonucleotide probes attached to a gel matrix.

The biotin-labeled cRNA target is prepared by a linear amplification method. Poly (A) + RNA (within the total RNA population) is primed for reverse transcription by a DNA oligonucleotide containing a T7 RNTA polymerase promoter 5' to a (dT) 24 sequence. After second-strand cDNA synthesis, the cDNA serves as the template in an in vitro transcription (IVT) reaction to produce the target cRNA. The IVT is performed in the presence of biotinylated nucleotides to label the target cRNA. This procedure results in a 50-200 fold linear amplification of the input poly (A) + RNA.

Hybridization Probes.

The oligonucleotide probes were provided by the Codelink Uniset Mouse I Bioarray (Amersham, product code 300013). Amine-terminated oligonucleotide probes are attached to a three-dimensional polyacrylamide gel matrix. There are 10,000 oligonucleotide probes, each specific to a well-characterized mouse gene. Each mouse gene is

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representative of a unique gene cluster from the fourth quarter 2001 Genbank Unigene build. There are also 500 control probes.

The sequences of the probes are proprietary to Amersham. However, for each probe, Amersham identifies the corresponding mouse gene by NCBI accession number, OGS, LocusLink, Unigene Cluster ID, and description (name). This information should be available from Amersham. In the case of the differentially expressed probes, this information is duplicated in master table 1. For the complete list, see http://www4.amershambiosciences.com/aptrix/upp01077.nsf/Content/codelink_literature

15 Under "Gene Lists", select "Uniset Mouse I", and a gene list, in Excel format, can be downloaded.

Hybridization

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Using the cRNA target, the hybridization reaction mixture is prepared and loaded into array chambers for bioarray processing as set forth in the manufacturer's instructions for CodeLink Gene Expression BioarraysTM (Amerhsam Biosciences). Each sample is hybridized to an individual microarray. Hybridization is at 37°C. The hybridization buffer is prepared as set forth in the Motorola instructions. Hybridization to the microarray is detected with an avidinated fluorescent reagent, Streptavidin-Alexa Fluor ® 647 (Amersham).

Mouse Gene Expression Analysis

Processed arrays were scanned using a GenePix 4000B Microarray Scanner (Axon Instruments, Inc.); array images were acquired using the Amersham CodeLink™ Analysis Software (Release 2.2). The Amersham CodeLink™ Analysis Software gives an integrated optical density (IOD) value for every spot; a unique background value for that spot is subtracted, resulting in "raw" data points. Individual chips are then normalized by the Amersham Codelink™ software according to the median raw intensity for all 10,000 genes. A negative

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control threshold (0.2) is also calculated according to the control probes. The expression data was analyzed to identify genes whose expression levels changed significantly with respect to:

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Normal mice compared to hyperinsulinemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

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Normal mice compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

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Hyperinsulinemic compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on high-fat diets.

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Database Searches Nucleotide sequences and predicted amino acid sequences were compared to public domain databases using the Blast 2.0 program (National Center for Biotechnology Information, National Institutes of Health). Nucleotide sequences were displayed using ABI prism Edit View 1.0.1 (PE Applied Biosystems, Foster City, CA).

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Nucleotide database searches were conducted with the then current version of BLASTN 2.0.12, see Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res., 25:3389-3402 (1997). Searches employed the default parameters, unless otherwise stated.

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For blastN searches, the default was the blastN matrix (1,-3), with gap penalties of 5 for existence and 2 for extension.

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Protein database searches were conducted with the thencurrent version of BLAST X, see Altschul et al. (1997), supra. Searches employed the default parameters, unless otherwise stated. The scoring matrix was BLOSUM62, with gap costs of 11 for existence and 1 for extension. The standard low complexity filter was used.

"ref" indicates that NCBI's RefSeq is the source database. The identifier that follows is a RefSeq accession

number, not a GenBank accession number. "RefSeq sequences are derived from GenBank and provide non-redundant curated data representing our current knowledge of known genes. Some records include additional sequence information that was never submitted to an archival database but is available in the literature. A small number of sequences are provided through collaboration; the underlying primary sequence data is available in GenBank, but may not be available in any one GenBank record. RefSeq sequences are not submitted primary sequences. RefSeq records are owned by NCBI and therefore can be updated as needed to maintain current annotation or to incorporate additional sequence information." See also http://www.ncbi.nlm.nih.gov/LocusLink/refseq.html

It will be appreciated by those in the art that the exact results of a database search will change from day to day, as new sequences are added. Also, if you query with a longer version of the original sequence, the results will change. The results given here were obtained at one time and no guarantee is made that the exact same hits would be obtained in a search on the filing date. However, if an alignment between a particular query sequence and a particular database sequence is discussed, that alignment should not change (if the parameters and sequences remain unchanged).

Northern Analysis.

Northern analysis may be used to confirm the results. Favorable and unfavorable genes, identified as described above, or fragments thereof, will be used as probes in Northern hybridization analyses to confirm their differential expression. Total RNA isolated from subject mice will be resolved by agarose gel electrophoresis through a 1% agarose, 1 % formaldehyde denaturing gel, transferred to positively charged nylon membrane, and hybridized to a probe labeled with [32P] dCTP that was generated from the aforementioned gene or fragment using the Random Primed DNA Labeling Kit (Roche, Palo Alto, CA), or to a probe labeled with digoxigenin (Roche Molecular Biochemicals,

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Indianapolis, IN), according to the manufacturer's instructions.

Real-Time RNA Analysis.

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Real-time RNA analysis may also be used for confirmation. For "real-time" RNA analysis, RNA will be converted to cDNA and then probed with gene-specific primers made for each clone. "Real-time" incorporation of fluorescent dye will be measured to determine the amount of specific transcript present in each sample. Sample differences (control vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or control vs. diabetic) will be evaluated. Confirmation using several independent animals is desirable.

15 In situ Hybridization

Another form of confirmation may be provided by nonisotopic in situ hybridizations (NISH) on selected human (obtained by Tissue Informatics) and mouse tissues using cRNA probes generated from mouse genes found to be up- or down-regulated during the disease progression. hybridizations may also be performed on mouse tissues using cRNA probes generated from differentially expressed DNAs. These cRNA's will hybridize to their corresponding messenger RNA's present in cells and will provide information regarding the particular cell types within a tissue that is expressing the particular gene as well as the relative level of gene expression. The cRNA probes may be generated by in vitro transcription of template cDNA by Sp6 or T7 RNA polymerase in the presence of digoxigenin-11-UTP (Roche Molecular Biochemicals, Mannheim, Germany; Pardue, M.L. In: In situ hybridization, Nucleic acid hybridization, a practical approach: IRL Press, Oxford, 179-202).

Transgenic Animals.

Transgenic expression may be used to confirm the results. In one embodiment, a mouse is engineered to overexpress the favorable or unfavorable mouse gene in question. In another embodiment, a mouse is engineered to express the

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corresponding favorable or unfavorable human gene. In a third embodiment, a nonhuman animal other than a mouse, such as a rat, rabbit, goat, sheep or pig, is engineered to express the favorable or unfavorable mouse or human gene.

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Hyperquantitative Tissue Analysis

In addition to gene expression analysis the tissue sections can also be analyzed using TissueInformatics, Inc.'s TissueAnalytics™ software. A single representative section may be cut from each tissue block, placed on a slide, and stained with H&E. Digital images of each slide may be acquired using an research microscope and digital camera (Olympus E600 microscope and Sony DKC-ST5). These images may be acquired at 20x magnification with a resolution of 0.64 mm/pixel. A hyperquantitative analysis may be performed on the resulting images: First a digital image analysis can identify and annotate structural objects in a tissue using machine vision. These objects, which are constituents of the tissue, can be annotated because they are visually identifiable and have a biological meaning. Subsequently a quantification of these structures regarding their geometric properties like area or stain intensities and their relationship to the field of view or per unit area in terms of a % coverage may be performed. Features or parameters for hyper-quantification are specific for each tissue, and may also include relations between features, measures of overall heterogeneity, including orientation, relative locations, and textures.

30 Correlation Analysis

Mathematical statistics provides a rich set of additional tools to analyze time resolved data sets of hyperquantitative and gene expression profiles for similarities, including rank correlation, the calculation of regression and correlation coefficients, and clustering. Continuous functions may also be fitted through the data points of individual gene and tissue feature data. Relation between gene expression and hyper-quantitative tissue data may be

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linear or non-linear, in synchronous or asynchronous arrangements.

Example 1

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Obesity is increasing at an alarming rate in the United States. In parallel, the incidence of type II diabetes is also rising. We are interested in defining alterations in gene expression that correlate with the development of these conditions in the hopes of reversing these dangerous trends.

Insulin plays a major role in regulating blood glucose levels. It stimulates the uptake of glucose in adipose tissue and striated muscle for storage as intracellular triglycerides and glycogen. Insulin also inhibits the release of glucose from the liver. Normally, this would prevent the rise in blood sugar concentration that occurs after eating. However, in the early stages of type 2 diabetes, resistance to insulin is seen.

Muscle plays a major role in glucose metabolism. Thus, it also is a major contributor to the development of type 2 diabetes. In normal situations, muscle cells respond to increasing levels of insulin by increasing glucose uptake from the bloodstream. However, during the very early stages of type 2 diabetes, muscle tissue becomes resistant to insulin, requiring the pancreatic beta cells to increase insulin secretion. Eventually, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and insulin production drops. Thus, clinical type 2 diabetes results from the combination of insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance (Petersen and Shulman, 2002). At least three steps - those mediated by glycogen synthase, hexokinase, and GLUT4 - have been reported to be defective in patients with type 2 diabetes. Fatty acids also can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase.

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We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat, an increasing component in the U.S. diet, and has been documented to lead to diabetes in C57BL/6J mice (Surwit et al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets.

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Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. RNA was extracted from the gastrocnemius muscle at each time point.

In order to identify additional muscle genes involved in the development of type 2 diabetes, we used microarray analysis to compare RNA expression levels of 10,000 genes in muscle of high fat diet fed and control diet fed mice at various time points in the progression of type 2 diabetes. Microarray analysis provides a more global picture of gene regulation, allowing the identification of families or groups of genes showing similar expression patterns that potentially imply similar or coordinated roles in disease progression.

Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

Of 10,000 genes analyzed, 121 were up-regulated but only 7 down-regulated greater than two-fold in the diabetic

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relative to non-diabetic mice. These genes are listed in Master Table 1.

This distribution of up- and down-regulated genes was much different from that seen for other organs (liver, pancreas, and white adipose tissue) where there was a much closer balance between the number of up- and down-regulated genes. Actin, alpha, cardiac (Actc1, NM_009608) was one of the most down-regulated genes when comparing HF to Std mice. It was consistently expressed at lower levels in the HF diabetic mice in comparison to the Std mice and also steadily decreased over the 16 week study.

Example 2

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Interestingly, further analysis of the time points and exploration of gene pathways and functionally related genes revealed a subset of actin-related and actin-binding genes exhibiting a consistent decrease in expression (although less than two-fold) in the diabetic mice; 9 of 37 functionally related genes were decreased in diabetic muscle at all four time points and an additional 9 were decreased at three of the four time points. Only two of these genes had been included in the original list of 7 down-regulated genes using the two-fold cut-off criterion.

It is possible that this subtle but coordinated down-regulation of actin-related or actin-binding genes reflects a role in the decreased glucose uptake by skeletal muscle that occurs in diabetes. With nearly half (18 of 37) of the genes in a related family of genes being consistently down-regulated in a study that did not identify a large number of down regulated genes, we feel that actin and genes in actin-related pathways may prove to play key roles in muscle as obesity and diabetes progress.

The actin-related and actin-binding mouse genes in question have been included at the end of Master Table 1, subtable 1A.

Introduction to Master Tables

The master tables reflect applicants' analysis of the gene chip data.

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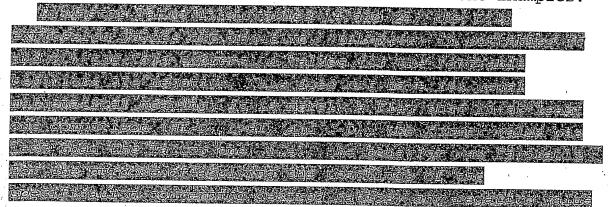
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For each probe corresponding to a differentially expressed mouse gene, Master Table 1 identifies

- Col. 1: The mouse gene (upper) and mouse protein (lower) database accession #s.
 - Col. 2: The corresponding mouse Unigene Cluster, as of the $4^{\rm th}$ Quarter 2001 build.
- 15 Col. 3: The behavior (differential expression) observed for the mouse gene. This column identifies the gene as favorable(F) or unfavorable (U) on the basis of its strongest differential behavior at the ages tested. There are three possible comparisons, HI-D, C-HI, and C-D, where C=control (normal), HI=hyperinsulinemic, and D=diabetic. If HI>D, C>HI, or C>D, the behavior for that subject comparison is considered unfavorable. If the inequality is reversed, the behavior for that subject comparison is considered favorable.
 - In the Master Table, the numerical value is the ratio of the greater value to the lesser value. If this ratio is at least two fold, the degree of differential expression is considered strong. Usually only mouse genes exhibiting at least one strong differential expression behavior are listed in the Master Table; exceptions are noted in the Examples.



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Victoria (Company)

Col. 4: A related human protein, identified by its database accession number. Usually, several such proteins are identified relative to each mouse gene. These proteins have been identified by BLAST searches, as explained in cols. 6-8.

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- Col. 5: The name of the related human protein.
- Col. 6: The score (in bits) for the alignment performed by the BLAST program.

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Col. 7: The E-value for the alignment performed by the BLAST program. It is worth noting that Unigene considers a Blastx E Value of less than 1e-6 to be a "match" to the reference sequence of a cluster.

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Unless otherwise indicated, the bit score and E-value for the alignment is with respect to the alignment of the mouse DNA of col. 1 to the human protein of col. 4 by BlastX, according to the default parameters.

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Master Table 1 is divided into three subtables on the basis of the behavior in col. 3. If a gene has at least one significantly favorable behavior, and no significantly unfavorable ones, it is put into Subtable 1A. In the opposite case, it is put into Subtable 1B. If its behavior is mixed, i.e., at least one significantly favorable and at least one significantly unfavorable, it is put into Subtable 1C. Note that this classification is based on the strongest observed differential expression behaviors for each of the three subject comparisons, C-HI, HI-D and C-D.

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The corresponding human gene clusters are also of interest. These may be obtained in a number of ways. First, one may

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search on Unigene

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(http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=unigene) for the identified human protein. Review the "hits" (each of which is a Unigene record) for those prefixed by "Hs." Secondly, one may access the Unigene record for the mouse gene cluster (which is given in Master Table 1), and then click on "Homologene". This will bring up a new page which includes the section "Possible Homologous Genes". One of the entries should be a Homo sapiens gene (considered by Unigene to be the most related human gene); click on its Unigene record link.

Additional information of interest may be accessed by searching with the mouse gene accession # in the Mouse Gene Informatics database, at http://www.informatics.jax.org/.

MASTER TABLE 1 SIGNIFICANTLY DIFFERENTIALLY EXPRESSED MOUSE GENES/PROTEINS AND CORRESPONDING HUMAN PROTEINS

Subtable 1A: Wholly Favorable Genes and Proteins

E-value		0	0	0	.0	0	205 8E-54	. [204 1E-53	204 2E-53	204 2E-53		204 2E-53	286 8E-78	286 8E-78	,	· .	286 8E-78	286 8E-78	286 8E-78	286 8E-78	286 8E-78	286 8E-78	286 8E-78	285 2E-77
Score (bits)	. 1711	1711	1711	1711	.1315	1276 0	205	100	204	204	204		204	286	286		,	987	286	286	-286	286	286	286	285
Human Protein Name	antigen identified by monoclonal antibody Ki-67; Proliferation-related Ki-67 antigen	KI67 HUMAN Antigen KI-67	cell proliferation antigen Ki-67, long form	antigen of the monoclonal antibody Ki-67	antigen of the monoclonal antibody Ki-67	cell proliferation antigen Ki-67, short form	GSK-3beta binding protein FRAT1	_	frequently rearranged in advanced 1-cell lymphomas	frequently rearranged in advanced T-cell lymphomas	FRT1_HUMAN Proto-oncogene FRAT1 (Frequently rearranged in advanced T-cell	lymphomas)	proto-oncogene	stathmin 1; metablastin; prosolin; oncoprotein 18; phosphoprotein 19; stathmin; leukemia-associated phosphonotein n18	STN1 HUMAN Stathmin (Phosphoprotein p19) (pp19) (Oncoprotein 18) (Op18)	(Leukerma-associated phosphoprotein p18) (pp17) (Prosolin) (Metablastin) (Pr22	protein)	stathmin	Pr22 protein	stathmin	oncoprotein 18	protein p18	Pr22	dJ125I3.1 (leukemia-associated phosphoprotein p18 (stathmin))	AAH14353 Similar to stathmin 1/oncoprotein 18
Human Proteins	NP_002408.2	P46013	A48666	CAA46519.1	CAA46520.1	B48666	BAB86352.1	4 7 PA CATA	AAH34476.1	NP 005470.1	Q92837	•	AAB97096.2	NP_005554.1	P16949			A40936	CAA77660.1	CAA37391.1	AAA59971.1	AAA59980.1	CAA64398.1	CAC16020.1	AAH14353.1
Behavior	F:(IR-D) -3.33						_																		ï
Unigene	Mm.4078				,		Mm.90135 F:(IR-D)							Mm.28479 F:(IR-D)											
Mouse Gene Protein	X82786 CAA58026.1			5		•	NM_013788 NP_038816.1	***************************************				, ,		NM_019641 NP_062615.1						·					

	-		O9H160	STN4 HTMAN Stathmin 4 (Stathmin-like protein B3) (RB3)	197	194 4E-50
	-		22254.1	RB3 protein	. 194	. 4E-50
	-		56503.1	hypothetical protein	194	4E-50
			10422.2	stathmin-like-protein RB3	197	194 4E-50
			AAH11520.1	AAH11520 Similar to stathmin-like-protein RB3	19	194 4E-50
NM_011623 Mm.4237	l	F:(IR-D)	01058.2	DNA topoisomerase II, alpha isozyme; topoisomerase (DNA) II alpha (170kD); DNA	2463 0	<u> </u>
NP_035753.1		33		topoisomerase II, 1/0 kU		
			P11388	TP2A HUMAN DNA topoisomerase II, alpha isozyme	2463 0	3 0
	\vdash		77388.1	topoisomerase II alpha	2463	3 0
	_	Ī	Т.	DNA topoisomerase II (EC 5.99.1.3)	2462	5 0
	\vdash		09762.1	DNA topoisomerase (ATP-hydrolysing); topoisomerase II alpha	2454 0	1 0
	-			DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) alpha	2441	0 1
				TP2B HUMAN DNA topoisomerase II, beta isozyme	192	1923 0
	_		A39242	DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) beta, splice form 2	1923 0	30
			NP_001059.2	DNA topoisomerase II, beta isozyme; topo II beta; DNA topoisomerase II, 180 kD; topoisomerase (DNA) II beta (180kD)	1923	0
			CAA48197.1	DNA topoisomerase II	1923	3 0 ·
	-		AAC77432.1	DNA topoisomerase II beta	1918	8 0
-	-		61210.1	topoisomerase Π	149	1494 0
	-				<u>:</u>	:
AK007688 Mm.4	Mm.41925 F:(IR-D)		NP_076947.1	hypothetical protein MGC2601	45	457 e-128
AAH37181.1	7	17.	:		1	
	-		CAB56188.1	c380A1.2.1 (novel protein (isoform 1))	457	7 e-128
	_		AAH00662.1	Unknown (protein for MGC:2601)	45	457 e-128
			AAK61247.1	AE006464 15 unknown	45	457 e-128
<u>.</u>	-		CAB56189.1	c380A1.2.2 (novel protein (isoform 2))	300	0 3E-81
NM_011593 Mm.8245	1	F:(IR-D)	CAA26443.1	EPA glycoprotein	27	270 1E-72
23.1	Υ,	2.18				
			NP_003245.1	tissue inhibitor of metalloproteinase 1 precursor; Erythroid-potentiating activity (tissue inhibitor of metalloproteinases): erythroid potentiating activity	27	270 1E-72
			P01033	TIM1_HUMAN Metalloproteinase inhibitor 1 precusor (TIMP-1) (Erythroid notentiating activity) (FPA) (Tissue inhibitor of metalloproteinases) (Fibroblast	27	270 1E-72
	1			powintaining acutaity) (11 123 to 11 11 12 to 11 11 11 11 11 11 11 11 11 11 11 11 11		

L				1.	L		
				collagenase inhibitor) (Collagenase inhibitor)	4		
		,	ZYHUEP	metalloproteinase tissue inhibitor 1 precursor [validated]		27011	1E-72
			26902.1	rosmosid		270 1E-72	E-72
			52436.1	prefibroblast collagenase inhibitor	· `	270 1E-72	E-72
			AAA63234.1	collagenase inhibitor		270 1E-72	E-72
,			14009.1	S68252 1 metalloproteinase inhibitor		270 1	1E-72
	:	:	100866.1	AAH00866 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity,	_	270 1	1E-72
				collagenase inhibitor)		1	
,		,	1107278A	erythroid potentiating activity	_	270	270 1E-72
			1308125A	metalloproteinase inhibitor		270 1E-72	E-72
			1UEA	B Chain B, Mmp-3TIIMP-1 Complex		264 8E-71	E-71
			1UEA	D Chain D, Mmp-3TIMP-1 Complex	<u>. </u>	264 8E-71	E-71
			BAA01913.1	tissue inhibitor of metalloproteinases	_	236 1	1E-62
			107097.1	AAH07097 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)		221	221 6E-58
T	Mm.10169	F:(IR-D)	NP_000358.1	000358.1 thiopurine S-methyltransferase	ļ	376 e-104	-104
1.C00000.1		-7.10	:				-
٠			P51580	TPMT HUMAN Thiopurine S-methyltransferase (Thiopurine methyltransferase)		376 e-104	-104
			I\$7946	thiopurine methyltransferase		376 e-104	-104
			AAB27277.1	thiopurine methyltransferase; TPMT		376 e	e-104
			AAC50130.1	thiopurine methyltransferase	_	376 e-104	-104
			AAC50368.1	thiopurine methyltransferase		376 e-104	-104
			AAC51865.1	thiopurine S-methyltransferase		376 e-104	-104
			BAA97037.1	thiopurine S-methyltransferase		376 e-104	-104
		•	AAH09596.1	AAH09596 thiopurine S-methyltransferase		376 e-104	-104
			AAB71630.1	thiopurine methyltransferase		375 e-104	-104
			AAB71626.1	thiopurine methyltransferase		375 e-104	-104
			AAB80746.1	thiopurine S-methyltransferase		374 e-103	-103
			AAB71629.1	thiopurine methyltransferase		374 e-103	-103
			AAB71627.1	thiopurine methyltransferase	•	373 €	e-103
		٠	AAH05339.1	AAH05339 thiopurine S-methyltransferase		372 €	e-103
		,	AAB71625.1	thiopurine methyltransferase		371	e-103
			AAB80747.1	thiopurine S-methyltransferase		371 e-130	-130

265 9E-84	5 6E-83	6 e-136	6 e-136	484 e-136		4 e-136	3 e-136	482 e-135	480 e-135	469 e-131	435 e-121	372 e-102	372 e-102	372 e-102	·	283 1E-75	283 1E-75	3 1E-75	282 2E-75	281 3E-75	246 2E-64	531 e-151		531 e-151	531 e-151	531 e-151	531 e-151
26	265	486	486	48		484	483	48	48	46	43	37	3.7	37		78	78	283	37	28	77 .	53		5	5.	5	5:
thiopurine methyltransferase	similar to thiopurine methyltransferase	CA11_HUMAN Collagen alpha 1(I) chain precursor	pro alpha 1(I) collagen	alpha 1 type I collagen preproprotein; Collagen I, alpha-1 polypeptide; osteogenesis imperfecta type IV; collagen of skin, tendon and bone, alpha-1 chain		prepro-alpha1(I) collagen	collagen alpha 1(I) chain precursor	alpha 1 (I) chain propeptide	Unknown (protein for MGC:33668)	type I collagen pro alpha 1(I) chain propeptide	_	pro-alpha 1 (II) collagen (313 AA; AA 975-271c)		alpha-1 type II collagen		prion gene complex, downstream	PRND HUMAN Prion-like protein doppel precursor (PrPLP) (Prion protein 2)	_	dJ1068H6.4 (prion protein like protein doppel)		AF187843_1 dopped protein	uncoupling protein 3, isoform UCP3L		UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)	uncoupling protein UCP3, mitochondrial	UCP3	uncoupling protein 3
AAC50129.1	XP 031946.2		AAB94054.2	NP_000079.1		CAA98968.1	CGHU1S	AAA51995.1	AAH36531.1	AAB27856.1	CAA29605.1	CAA29604.1	NP_001835.2	AAC41772.1		NP_036541.1	Q9UKY0	AAF02424.1	CAB75502.1	AAG43449.1	AAG43448.1	NP_003347.1		P55916	JC5522	AAC51367.1	AAC51369.1
		i !		-			·					,				F:(RD) -2.14						F:(IR-D) -2.07					
		Mm.22621 F:(IR-D) -2.16		٠	*							,	,			Mm.18075 F:(IR-D) 0 -2.14					,	Mm.6254					
		U08020 AAA88912.1		-	,		1				ţ		, .			NM_023043 NP_075530.1	-		ţ			NM_009464	NP 033490.1		_	,	

AACS1767.1 uncoupling protein-3 531 e-151		W	'O :	200)5/U		398	•			. •		:				11	8							P'	CT/U	S2	00
AAG02284.1 ARG50113_1 uncoupling protein-3 AAG02284.1 AAG02284.1 AAG02284.1 AAG02284.1 AAG02284.1 AAG02284.1 AAG0113_2 uncoupling protein-3 S31	≥151	3-151	9-149	≻144	3-131	3-131 ·	3-129	3-128.	3-128	 	€-128	e-128	e-128	e-128	e-128	e-128	7E-95	7E-95	7E-95	6E-94	6E-94	2E-55	9E-84		2E-76	2E-76		2E-76
AAG02284.1 AAG02284.1 AAC51785.1 NP 073714.1 AAB48411.1 NP 003346.2 AAC51356.1 AAD21151.1 AAB53091.1 CAA11402.1 AAB53091.1 CAA11402.1 NP 068605.1 GAA1402.1 AAAB53091.1 CAA1402.1 AAAB53091.1 CAA11402.1 AAAB53091.1 CAA11402.1 AAAB53091.1 CAA11402.1 AAAB53091.1 CAA11402.1 AAAB53091.1 AAAB53091.1 AAAB53091.1 AAAB53091.1 AAAB53091.1 AAAB53091.1 AAAB530.1 AAAB530.1 AAAB530.1 AAAB530.1	531	531 (525	. 510	464 €	464	457	456	456		456	456	456	456	456	456	345	345	345	342	342	214	608		285	285		2851
AAC51767 AAG02284 AAC18822 AAC51785 NP 073714 AAB48411 NP_003346 AAC51336 AAC51336 AAC51336 AAC51336 AAC51336 AAC51336 AAC51336 AAC51336 AAC51336 AAAC51336 AAAB53091 CAA11402 NP 06860 G01858 AAA85271 P25874 CAA168397 Mm.10557 F:(IR-D) CAC07336 1 AAK9953	uncoupling protein-3	AF050113_1 uncoupling protein-3	uncoupling protein 3	uncoupling protein 3	uncoupling protein 3, isoform UCP3S	UCP3S	uncoupling protein-2	_	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP 2) (UCPH)		UCP2	uncoupling protein 2	uncoupling protein-2	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)	uncoupling protein homolog	uncoupling protein 2	uncoupling protein 1; mitochondrial brown fat uncoupling protein	uncoupling protein 1, mitochondrial	uncoupling protein	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	uncoupling protein	AAH08392 Similar to uncoupling protein 3 (mitochondrial, proton carrier)	dJ137F1.2 (novel member of the potassium channel subfamily K)		potassium channel, subfamily K, member 16; pancreatic 2P domain potassium channel	CIWG HUMAN Potassium channel subfamily K member 16 (TWIK-related alkaline	LI ACLIVATOU N.T CHAILLEI 1) (LF UOMAIN POTASSIUM CHAINTEL LAIK-1)	AF358909 1 2P domain potassium channel Talk-1
Mm.10557 F:(TR-D)	AAC51767.1	AAG02284.1	AAC18822.1	AAC51785.1	NP 073714.1	AAC51356.1	AAB48411.1		P55851		AAC51336.1	AAC39690.1					NP 068605.1	G01858	AAA85271.1	P25874	CAA36214.1	AAH08392.1	CAC07336.1	,		096T55	7 000007	AAK49532.1
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																		· :					Mm.10557		,	-		,
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255 SE-67	:	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	255 5E-67	254 1E-66	250 2E-65	250 2E-65	249 3E-65	249 3E-65	223 2E-57	448 e-125	115 a 175	446 e-125	446 e-125	446 e-125	446 e-125	446 e-125	446 e-125
000603.1 insulin-like growth factor 2 (somatomedin A); somatomedin A		IGF2_HUMAN Insulin-like growth factor II precursor (IGF-II) (Somatomedin A)	nsulin-like growth factor II precursor [validated]	IGF-II precursor	precursor polypeptide (AA -24 to 156)	preproinsulin-like growth factor II, domains A-E	insulin-like growth factor	insulin-like growth factor II precursor		insulin-like growth factor II; IGF-II	AF217977 1 unknown	AAH00531 insulin-like growth factor 2 (somatomedin A)	AF517226 insulin-like growth factor 2 (somatomedin A)	insulin-like growth factor II precursor	insulin-like growth factor II	insulin-like growth factor II precursor		preproinsulin-like growth factor II, domains A-E	insulin-like growth factor II precursor, splice form II		precursor polypeptide (AA -24 to 140)		ceroid_linofiscinosis neuronal 8 (enilensy progressive with mental retardation)	$\overline{}$	AF123757 1 putative transmembrane protein			AF123760 1 putative transmembrane protein	
NP_000603.1		P01344	IGHU2	CAA25426.1	CAA29516.1	AAA52442.1	AAA52535.1	AAA52545.1	AAA60088.1	AAB34155.1	AAG17220.1	AAH00531.1	AAM51825.1	1009249A	1203258B	AAA52544.1	167610	AAA52443.1	S02423	CAA27249.1	CAA29517.1	AAH07725.1	NP 061764 1	Q9UBY8	AAF13115.1	AAF13116.1	AAF13117.1	AAF13118.1	AAF13119.1
Mm.3862 F:(R-D) -2.06										, , mare		,										Mm.21578 F:(IR-D) -2.09							
NM_010514 NP_034644.1	1					,							-	· ·		-			1			NM_012000 NP_036130.1	,				,		

345 2E-94	345 2E-94	342 1E-93	342 1E-93	342 1E-93	347 1E-03	249 1E-65	249 1E-65	249 1E-65	249 IE-65	249 1E-65	248, 2E-65	245 2E-65	217 5E-56	217 SE-56	217 SE-56	206 7E-53	206 7E-53	0 808	÷	807 0	0 208	. 0 208	507 e-143	499 e-140	499 e-140	499 -140
similar to data source:MGD, source key:MGI:98241, evidence:ISS~putative~superiorcervical ganglia, neural specific 10	AAH06302 Similar to superiorcervical ganglia, neural specific 10		┪	STN2_HUMAN Stathmin 2 (SCG10 protein) (Superior cervical ganglion-10 protein)	cilanoar alamani	7-	1	SCG1(bK3184A7.2 (SCG10-like protein (SCLIP) (ortholog of rabbit neuroplasticin-2 (NPC2)))	AAH09381 Unknown (protein for MGC:16668)		unnamed protein product	STN4 HUMAN Stathmin 4 (Stathmin-like protein B3) (RB3)	1	hypothetical protein	stathmin-like-protein RB3		Similar to nuclear factor I/B		nuclear factor I/B	NFIB_HUMAN Nuclear factor 1 B-type (Nuclear factor 1/B) (NF1-B) (NF1-B) (NF-I/B) (CCAAT-box binding transcription factor) (CTF) (TGGCA-binding protein)	nuclear factor I-B2	nuclear factor 1 B-type	nuclear factor I/C (CCAAT-binding transcription factor)		nuclear factor I/C (CCAAT-binding transcription factor)
XP_170521.1	AAH06302.1	NP_008960.1	AAB36428.1	Q93045	BA A73376 1	NP 056978.2	Q9NZ72	AAF35245.1	CAC16222.1	AAH09381.1	AAD12730.1	BAC11252.1	Q9H169	CAC22254.1	CAB66503.1	NP 110422.2	AAH11520.1	AAH01283.1		NP 005587.1	000712	AAB41899.1	AAA93125.1	NP 005588.1	CAA63440.1	AAH12120.1
				-														F:(C-IR)	-2.69						·	
Mm.29580 F:(C-IR)		,		-	•								·	:				Mm.4025					;		,	,
NM_025285 NP_079561.1			·	٠									-					NM_008687	NP 032713.1	٠		,			,	

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487 e-137	e-136	484 e-136	e-136	• •	400	e-150	483 e-136	334 2E-91	4E-89	4E-89	317 2E-86	284 2E-76	2E-76	e-111	• • •	e-1111	e-111	402 e-111	e-111	402 e-111	e-101		e-101	e-101	e-101	365 e-101	365 e-101
487	484	484	483		5	483	483	334	326	326	317	284	284	402		402	402 e-111	402	402	402	365	:	365	365	365	365	365
NFIC_HUMAN Nuclear factor 1 C-type (Nuclear factor 1/C) (NF1-C) (NF1-C) (NF-I/C) (CCAAT-box binding transcription factor) (CTF) (TGGCA-binding protein)	nuclear factor I	KIAA1439 protein	NFIA_HUMAN Nuclear factor 1 A-type (Nuclear factor 1/A) (NF1-A) (NF1-A)	I/A) (CCAAT-box binding transcription factor) (CTF) (TGGCA-binding protein)	_	-	Nuclear Factor IA	SELT_HUMAN Selenoprotein T	selenoprotein T		similar to Selenoprotein T	Unknown	Unknown (protein for MGC:45090)	TERA protein		hypothetical protein DKFZp762L137.1	hypothetical protein	AF212220 1 TERA	unnamed protein product	AAH00024 TERA protein	TPM3_HUMAN Tropomyosin alpha 3 chain (Tropomyosin 3) (Tropomyosin gamma)		similar to tropomyosin, fibroblast	tropomyosin NM, skeletal muscle	skeletal muscle tropomyosin (AA 1-285)	AAH08407 Unknown (protein for MGC.14532)	AAH08425 Unknown (protein for MGC:14582)
P08651	B33416	BAA92677.1	Q12857	•		XP 046827.7	AAH22264.1	EIZN6Ò	NP 057359.1	AAF13696.1	XP 088553.	AAD20063.1	AAH36738.1	NP_067061.1		T46918	CAB75656.1	AAF87322.1	BAB15592.1	AAH00024.1	P06753		XP 036829.5	A24199	CAA27798.1	AAH08407.1	AAH08425.1
`,								4						F:(C-IR)	-2.4							75.7-		-	·		
			;	•			. ;	Mm.28026 F:(C-IR)						Mm.18637 F;(C-IR)	,						Mm.17306 F:(C-IR)	-					
			,		1			AK013022 Q9NZJ3				٠	,	NM_019643	NP_062617.1						NM_022314	T.CO/T/O_TAT					

			1900000		,	10.	[
		,	1209280A	tropomyosun	ان	305 e-101	j
			P09493	TPM1_HUMAN Tropomyosin 1 alpha chain (Alpha-tropomyosin)	ζ,	345 8E-95	5
	ţ		A25825	tropomyosin alpha chain, cardiac and skeletal muscle	3	345 8E-95	5
			AAA61225.1	skeletal muscle tropomyosin	3	345 8E-95	5
			P07951	TPM2_HUMAN Tropomyosin beta chain (Tropomyosin 2) (Beta-tropomyosin)	. 3	326 3E-89	6
			S00922	tropomyosin beta, skeletal muscle	3	326 3E-89	65
			CAA29971.1	beta-tropomyosin (AA 1-284)	3	326 3E-89	9
			133.1	AAH07433 Similar to tropomyosin 1 (alpha)	3	325 7E-89	6
	i		NP 689476.1	tropomyosin 3	. 3	315 9E-86	يو
	**	:	BAC03946.1	unnamed protein product	. 3	315 9E-86	92
			AAA61226.1	skeletal muscle tropomyosin	9 : 3	310 2E-84	34
			BAB14554.1	unnamed protein product	3	300 2E-81	
			NP 000357.2	tropomyosin 1 (alpha)	2	281 1E-75	75
			A27674	tropomyosin 3, fibroblast	. 2	281 1E-75	75
			AAA36771.1	шѕо⁄сшоdол	7	281 IE-75	75
			708796	uisoymodon	- 2	278 1E-74	74
,			CAB43309.1	hypothetical protein	1	278 1E-74	74
NM_011825 NP_035955.1	Mm.25760 F:(C-IR) -2.24	_	914.1	hypothetical protein FLJ21195 similar to protein related to DAC	<u>.</u>	308 SE-83	33
·						,	
			BAB15026.1	unnamed protein product	3	308 5E-83	33
,							
NM_009831	Mm.2103	F:(C-IR)	NP_004051.1	cyclin G1	5	543 e-154.	4
NP 033961.1	٠	7.7-			1	·	
1		,	P51959	CGG1_HUMAN Cyclin G1 (Cyclin G)	2	543 e-154	4
			G02401	cyclin G1	5	543 e-154	4
		·	AAC41977.1	cyclin G1	5	543 e-154	4
,			AAC50688.1	cyclin G1	5	543 e-154	4
				cyclin G	2	543 e-154	4
			H00196.1	cyclin G1	5	543 e-154	4
				cyclin G1	5	543 e-154	4
			AAH07093.	cyclin G1	i.c.	541 e-154	4
	,						١

			BAA13007 1	ryclin (r	517	514 e-146
			54821.1	cyclin G1	46,	462 e-130
			\vdash	cyclin G	421	e-117
-			1	cyclin G	421	e-117
			1	Similar to cyclin G2	292	8E-79
			_	cyclin G2	292	8E-79
			Q16589	CGG2_HUMAN Cyclin G2	292	8E-79
			AAC41978.1	cyclin G2	29,	292 8E-79
			AAC50689.1	cyclin G2	29;	292 8E-79
			AAN40704.1	cyclin G2	29.	292 8E-79
_			2210321B	cyclin G2	73	292 8E-79
NM_021282_N NP_067257_1	Mm.21758 F:(C-IR)		NP_000764.1	cytochrome P450, subfamily IIE, polypeptide 1; microsomal monooxygenase; xenobiotic monooxygenase: flavoprotein-linked monooxygenase: cytochrome P450.	792	7 0
1.102/00		F:(C-D) - 2.5		subfamily IIE (ethanol-inducible)		
			P05181	CPE1 HUMAN Cytochrome P450 2E1 (CYPIIE1) (P450-J)	. 792	2 0
			A31949	cytochrome P450 2E	792	2 0
			AAA52155.1	cytochrome P450IIB1	79	792 0
			AAA35743.1	cytochrome P450j	79	792 0
			AAF13601.1	AF182276 1 cytochrome P450-2E1	. 79	790 0
			AAD13753.1	cytochrome P450 2E1	751	1 0
			NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19;	. 557	7 e-158
. ,	ę t	`.		mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavonrotein-linked monooxygenase	· ·	
			P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYPIIC19) (P450-11A) (Mephenytoin 4-	.557	7 e-158
				hydroxylase) (CYPIIC17) (P450-254C)		1
			AAB59426.1	cytochrome	557	7 e-158
			NP_000763.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18;	35.	556 e-158
· :				cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase		
			AAB59356.1	cytochrome	55	556 e-158
			P33260	CPCI_HUMAN Cytochrome P450 2C18 (CYPIIC18) (P450-6B/29C)	553	3 e-157
			A61269	cytochrome P450 2C18	553	3 e-157
,			AAA02630.1	cytochrome P-4502C18	55	553 e-157

								:				12 4	ļ.	,						<i>.,</i> 0 c	,00,
550 e-156	550 e-156	e-156	550 e-156	550 e-156	e-156	e-155	9E-69		258 9E-69	258 9E-69.	258 9E-69	4E-68	0		0	0	0	0	0		0
550	550	250	250	. 550	550	545	. 258		258	258	258	256	2244		2244	. 2244	2244	1628 0	1628	1628 0	1628
cytochrome P-450	cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	CPC9_HUMAN Cytochrome P450 2C9 (CYPIIC9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)	S-mephenytoin 4-hydroxylase (EC 1.14.14) cytochrome P450 2C9	cytochrome P450	S-mephenytoin 4'-hydroxylase (EC 1.14.14) cytochrome P450 2C19	cytochrome P-450			polymerase (RNA) III (DNA directed) polypeptide K (12.3 kDa)	hypothetical protein FLJ22940	AE006462 3 Minus -99 protein	unnamed protein product			KPB1_HUMAN Phosphorylase B kinase alpha regulatory chain, skeletal muscle isoform (Phosphorylase kinase alpha M subunit)	phosphorylase kinase (EC 2.7.1.38) alpha-1 chain	phosphorylase kinase	phosphorylase kinase, alpha 2 (liver); Phosphorylase kinase deficiency, liver (glycogen storage disease; phosphorylase kinase, alpha 2 (liver), glycogen storage disease IX	KPB2_HUMAN Phosphorylase B kinase alpha regulatory chain, liver isoform (Phosphorylase kinase alpha L subunit)	phosphorylase kinase	phosphorylase kinase alpha subunit
BAA00123.1	NP_000762.2	P11712	B38462	1313295A	F38462	AAB23864.2	NP_078847.1		AAH01381.1	AAH09179.1	AAK61211.1	BAB15505.1	NP_002628.1		P46020	I38111	CAA52083.1	NP_000283.1	P46019	CAA56662.1	BAA07606.1
							F:(C-IR)	-2.19					F:(C-IR) -2.18	} !			;	,	r	,	
		·		,			Mm.29952 F:(C-IR)	. !					Mm.42254 F:(C-IR)					• 1.		- 1-	
					·		AK019452	BAB31728.1					NM_008832	NP_032858.1	·				1		

			1,7000		1678	_
			AAD32846.1		10701	
,			AAH14036.1	AAH14036 Similar to phosphorylase kinase, alpha 2 (liver)	1624 0	
	ļ .		86408.1	dJ499B10.2 (phosphorylase kinase, alpha 2 (liver) (PYK))	631	e-180
		,	27307.1	phosphorylase kinase alpha subunit liver isoform, PHKA2 {EC 2.7.1.38} [human, hepatoma, Peptide Partial, 377 aa]	473	e-132
			S74251	phosphorylase kinase (EC 2.7.1.38) beta chain	461	e-129
			33657.1	Similar to phosphorylase kinase, beta	461	e-129
	Mm.30006 F:(C-IR)	F:(C-IR)	96537.1	hypothetical protein	465	465 e-131
NP_076320.1	•	-2.16				
			CAB66868.1	hypothetical protein	465	e-131
	T		11647.1	AAH11647 Similar to hypothetical protein	465	e-131
			112802.1	AAH12802 Similar to hypothetical protein	465 e-13]	e-131
			AAH22856.1	hypothetical protein	465	465 e-131
٠			NP 064538.2	hypothetical protein FLJ21827	465	465 e-131
			BAB15146.1	unnamed protein product	465	465 e-131
AK004839 Mm.	Mm.2605	F:(C-IR)	NP_006735.1	retinol-binding protein 4, plasma precursor	343	343 2E-94
XP 129259.1		-2.15				:
			pir VAHU	plasma retinol-binding protein precursor	- 343	2E-94
			CAA24959.1	precursor RBP	343	2E-94
			P02753	Plasma retinol-binding protein precursor (PRBP) (RBP) (PRO2222)	341	1E-93
			AAH20633.1	Similar to retinol binding protein 4, plasma	341	1E-93
			XP 005907.5	similar to Plasma retinol-binding protein precursor (PRBP) (RBP) (PRO2222)	341	1E-93
			1RBP	Retinol Binding Protein	340	340 2E-93
			1BRP	Retinol Binding Protein (Holo Form)	340	340 2E-93
			1BRQ .	Retinol Binding Protein (Apo Form)	340	340 2E-93
			1401251A	retinol binding protein	340	340 2E-93
	,		10АВ	E Chain E, The Structure Of Human Retinol Binding Protein With Its Carrier Protein Transfluretin Reveals Interaction With The Carboxy Terminus Of Rhn	328	328 9E-90
	1		1QAB	F Chain F, The Structure Of Human Retinol Binding Protein With Its Carrier Protein	328	328 9E-90
	:			Transthyretin Reveals Interaction With		
			,	The Carboxy Terminus Of Rbp		• :
			A A F 69622.1	AF119917 30 PRO2222	288	288 6E-78

			, 00,000	CLEDITA	210	212 ST 55
			AAC03462.1	BAF	7.7	5.7
	-	1	043474	KLF4 HUMAN Kruppel-like factor 4 (Epithelial zinc-finger protein EZF) (Gut-	215	213 5E-55
			,	enriched Krueppel-like factor)		
			AAD42165.1	AF105036 1 zinc finger transcription factor GKLF	213	
		·	AAH29923.1	Kruppel-like factor 4 (gut)	213	5E-55
		,	NP 004226.1	Kruppel-like factor 4 (gut); endothelial Kruppel-like zinc finger protein	213	5E-55
		1.	AAB48399.1	hezh	213	5B-55
			AAH30811.1	Similar to Kruppel-like factor 4 (gut)	213	5E-55
			AAH35342.1	Similar to Kruppel-like factor 2 (lung)	211	3E-54
NM_020007 NP_064391_1	Mm.14199 F:(C-IR)	F:(C-IR)	AAK94915.1	AF401998_1 muscleblind 41kD isoform	695	e-166
1.1.C.L.O	,				:	
			NP 066368.1	muscleblind (Drosophila)-like	546	5 e-160
			BAA24858.1	KIAA0428	. 546	5 e-160
			Q9NR56	MBNL_HUMAN Muscleblind-like protein (Triplet-expansion RNA-binding protein)		537 e-157
			CAA74155.1	MBNL protein	53	537 e-157
			NP 659002.1	muscleblind-like protein MBLL39 isoform 1	44	449 e-125
			AAM09798.1	AF491866 1 muscleblind-like protein MLP1	44	449 e-125
,	·	1 13.	AAM50085.1	muscleblind-like protein MBLL39	. 427	7 e-119
,			NP 060858.2	CHCR isoform G	387	7 e-106
		,	Q9NUK0	MBXL_HUMAN Muscleblind-like X-linked protein (Cys3His CCG1-required protein) (HCHCR protein)	38	387 e-106
			AAL65661.1	CHCR isoform G	387	7 e-106
		**	BAB85648.1	hCHCR-G	-387	7 e-106
			CAD20869.1	CHCR protein	387	7 e-106
			AAM09533.1	AF491305_1 MBLX39	387	7 e-106
			NP 005748.1	muscleblind-like protein MBLL39 isoform 2	377	7 e-103
-			AAC67242.1	zinc finger protein	377	7 e-103
			BAB85649.1	hCHCR-R	343	3 1E-93
•			CAD20870.1	CHCR protein	343	3 1E-93
٠			AAL87670.1	AF467070 1 Cys3His CCG1-required protein isoform R	343	3 1E-93
			AAK82889.1	AF395876 1 36 kDa muscleblind protein EXP36	. 28	286 7E-82
NM 009883	Mm.4863	F:(C-IR)	CAC14276.1	bA112L6.1 (CCAAT/enhancer binding protein (C/EBP), beta)	27	271 2E-72

AAH07538.1 AAH107538.1 AAH21931.1 AAN86350.1 NP_005185.1 NP_005185.1 NP_005185.1 CAA36794.1 NP_01620.2 CAA36441.1 -2.02 NP_01620.2 A39824 AAA35845.1 1603359A Mm.38888 F:(C-IR) AAH11171.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 NP_000053.1	-						
AAH07538.1 AAH21931.1 AAN86350.1 NP_005185.1 NP_005185.1 S12788 CAA36794.1 F:(C-IR) CAA36794.1 CAA36794.1 F:(C-IR) AAA35845.1 I603359A AAA35845.1 I603359A THUC1 CAA38358.1		;	-2.03	,			
AAL55792.1 AAH21931.1 AAN86350.1 NP_005185.1 NP_005185.1 P17676 P17676 CAA36794.1 -2.02 R20292 P20292 P202922 P202922 P202922 P202922 P202922 P202922 P202922 P202922 P202922				AAH07538.1	Unknown (protein for MGC:15409)	271	2E-72
AAH21931.1 AAN86350.1 NP_005185.1 P17676 P17676 CAA36794.1 -2.02 R20292 P20292 P20292 R20292 A39824 AAA35845.1 1603359A F:(C-IR) AAH11171.1 -2.02 CAA38358.1 CAA38358.1 CAA30314.1 AAM21515.1 NP_000053.1				AAL55792.1	AF289608_1 unknown	.271	271 2E-72
AAN86350.1 NP_005185.1 P17676 P17676 S12788 S12788 CAA36794.1 -2.02 P20292 P20292 P20292 A39824 AAA35845.1 IG03359A F:(C-IR) AAA35845.1 IG03359A CAA38358.1				AAH21931.1	Unknown (protein for MGC.32080)	. 271	2E-72
Mm.19844 F:(C-IR) CAA36441.1 Mm.19844 F:(C-IR) CAA36441.1 Am.38888 F:(C-IR) AAA35845.1 IMM.38888 F:(C-IR) AAH11171.1 CAA38358.1	-		_	AAN86350.1	CCAAT/enhancer binding protein (C/EBP), beta	271	271 2E-72
Mm.19844 F:(C-IR) CAA36794.1 Mm.19844 F:(C-IR) CAA36441.1 -2.02 NP_001620.2 R20292 R20292 R39824 AAA35845.1 IG03359A Mm.38888 F:(C-IR) AAH11171.1 -2.02 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 NP_000053.1				NP_005185.1	CCAAT/enhancer binding protein (C/EBP), beta; CCAAT/enhancer-binding protein	271	271 2E-72
Mm. 19844 F.(C-IR) CAA36794.1 Mm. 19844 F.(C-IR) CAA36441.1 -2.02 NP_001620.2 RA39824 AAA35845.1 IG03359A Mm. 38888 F.(C-IR) AAH11171.1 -2.02 P05155 ITHUC1 CAA38358.1 CAA30314.1 AAM21515.1 NP_000053.1		,	,	•	(C/EBP), beta (transcription factor-5)		
Mm.19844 F:(C-IR) CAA36441.1 Am.19844 F:(C-IR) CAA36441.1 -2.02 NP_001620.2 R20292 R20292 R39824 AAA35845.1 1603359A Mm.38888 F:(C-IR) AAH11171.1 -2.02 CAA38358.1 CAA38358.1 CAA38358.1 CAA30314.1 AAMZ1515.1 NP_000053.1		``		P17676	CEBB_HUMAN CCAAT/enhancer binding protein beta (C/EBP beta) (Nuclear factor NF-IL6) (Transcription factor 5)	271	2E-72
Mm.19844 F.(C-IR) CAA36794.1 -2.02 NP_001620.2 NP_001620.2 A39824 AAA35845.1 1603359A Mm.3888 F.(C-IR) AAH11171.1 -2.02 ITHUC1 CAA38358.1 CAA38358.1 CAA30314.1 AAMZ1515.1 NP_000053.1 NP_000053.1 AAB59387.1 AAB59387.1	Т	,		S12788	transcription factor NF-IL6	271	2E-72
Mm.19844 F:(C-IR) CAA36441.1 -2.02 NP_001620.2 RA39824 AAA35845.1 Mm.38888 F:(C-IR) AAH11171.1 -2.02 ITHUC1 CAA38358.1 CAA30314.1 CAA30314.1 AAMZ1515.1 NP_000053.1 NP_000053.1 NP_AB59387.1	<u> </u>			CAA36794.1	nuclear factor NF-IL6 (AA 1-345)	. 271	2E-72
Mm.3888 F:(C-IR) AAH11171.1 Am.3888 F:(C-IR) AAH11171.1 -2.02 P05155 ITHUC1 CAA38358.1 CAA38358.1 CAA38358.1 AAM21515.1 NP_000053.1	· ·	Mm.19844	F:(C-IR) -2.02	36441.1	five-lipoxygenase activating protein (FLAP)	282	282 4E-76
Mm.38888 F:(C-IR) AAH11171.1 -2.02 P05155 THUC1 CAA30314.1 CAA30314.1 AAM21515.1 NP_000053.1 AAB59387.1				NP_001620.2	arachidonate 5-lipoxygenase-activating protein; five-lipoxygenase activating protein; MK-886-binding protein	282	4E-76
AA9924 AAA35845.1 I603359A I6033888 F:(C-IR) AAH11171.1 -2.02 P05155 ITHUC1 CAA30314.1 CAA30314.1 AAMZ1515.1 NP_000053.1			· \$	P20292	FLAP_HUMAN 5-lipoxygenase activating protein (FLAP) (MK-886-binding protein)	282	282 4E-76
Mm.38888 F:(C-IR) AAH11171.1 -2.02 P05155 ITHUC1 CAA38358.1 CAA38358.1 CAA30314.1 AAM21515.1 NP_000053.1 AAB59387.1				A39824	5-lipoxygenase-activating protein	282	282 4E-76
Mm.38888 F:(C-IR) AAH11171.1 -2.02 P05155 TTHUC1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 CAA38358.1 NP_000053.1				AAA35845.1	5-lipoxygenase activating protein	282	282 4E-76
Mm.38888 F.(C-IR) AAH11171.1 -2.02 P05155 ITHUC1 CAA38358.1 CAA30314.1 AAM21515.1 INP_000053.1 AAB59387.1				1603359A	Lipoxygenase activating protein	275	279 3E-75
P05155 ITHUC1 CAA38358.1 CAA30314.1 AAM21515.1 NP_000053.1	,	Mm.38888	F:(C-IR) -2.02	AAH11171.1	serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor),member 1	634	0
55 JC1 38358.1 30314.1 121515.1 000053.1 59387.1							
38358.1 30314.1 121515.1 000053.1 59387.1					IC1_HUMAN Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh)	633	. 0
38358.1 30314.1 121515.1 000053.1 59387.1				ITHUC1	complement C1 inhibitor precursor [validated	633	0
30314.1 121515.1 000053.1 59387.1				CAA38358.1	C1 inhibitor	633 0	0
421515.1 000053.1 59387.1		•		CAA30314.1	C1 inhibitor	633	0
59387.1		;		AAM21515.1	AF435921_1 C1 esterase inhibitor	633	0
59387.1		·		NP_000053.1	complement component 1 inhibitor precursor; serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor), member 1	. 632	0
	П	·			plasma protease (C1) inhibitor precursor	632 0	0

632 0	17 e-146	454 e-127	307 3E-83	930 0		930 0	927 0	927 0	927 0	927 0	927 0	927 0	817 0	1268 0	,	1268 0	1268 0	1266 0	1266 0	1266 0	1071 0	684 0	624 e-178	320 8E-87	;	435 e-122	
. 63	- 517	45	.3(6		6	6	6	6	9,	9,	9,	8	12	1 .	12	12,	12,	12	.12	10	9	9.	3		4	
plasma protease (C1) inhibitor precursor	C1 inhibitor (AA 155-478) (1 is 2nd base in codon)	C1-inhibitor	C1 inhibitor	similar to polymeric immunoglobulin receptor		hepatocellular carcinoma associated protein TB6	polymeric immunoglobulin receptor	PIGR_HUMAN Polymeric-immunoglobulin receptor precursor (Poly-IG receptor)	Secretory Component precursor [Validated]	transmembrane secretory component; poly-Ig receptor; SC	transmembrane secretory component; SC; poly-Ig receptor	Polymeric immunoglobulin receptor	poly-Ig receptor	glycerol-3-phosphate dehydrogenase (EC 1.1.99.5), mitochondrial precursor		glycerol-3-phosphate dehydrogenase	glycerol-3-phosphate dehydrogenase			mitochondrial glycerol-3-phosphate dehydrogenase	AF311325 1 glycerol-3-phosphate dehydrogenase 3	glycerol-3-phosphate dehydrogenase	AAH19874 Similar to glycerol-3-phosphate dehydrogenase 2 (mitochondrial)			myeloid leukemia factor 1	
AAA35613.1	130469.1		AAA51849.1	052013.1		AAN65630.1	NP 002635.1	P01833	ORHUGS	AAB20203.1	AAB23176.1	CAA51532.1	AAA36102.1	G02093		AAB60403.1	AAC50556.1	NP 000399.1	P43304	AAA65701.1	A'AG33851.1	AAB50200.1	AAH19874.1	XP_092005.2		NP_071888.1	
				F:(C-IR)	70.7-		÷							图	-2.01							,				F:(C-IR)	1
				Mm.4317	;			-						Mm.3711				:								Mm.10414 F:(C-IR)	
				1	INF_055212.1	٠				1					NF_034404.1	,				,						NM_010801 NP_034931_1	111111111111111111111111111111111111111

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435 e-122	435 e-122	435 e-122	396 e-110	e-106	e-135		e-135	e-135	482 e-135		482 e-135	482 e-135	482 e-135	e-135	e-135	482 e-135	482 e-135	482 e-135	e-135	e-135	481 e-135	481 e-135	481 e-135	e-135	e-135		e-135	481 e-135	481 e-135
435	435	435	396	383	482		482	482	482		482	482	482	482	482	482	482	482	482	481	481	481	481	481	481		481	481	481
MLF1_HUMAN Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1)	t(3;5)(q25.1;p34) fusion gene		unnamed protein product	unnamed protein product	bA525O21.1 (coagulation factor XIII, A1 polypeptide)		A Chain A, Recombinant Human Cellular Coagulation Factor Xiii	B Chain B, Recombinant Human Cellular Coagulation Factor Xiii	A Chain A, Coagulation Factor Xiii (A-Subunit Zymogen) (E.C.2.3.2.13) (Protein-	Gilitarinie Garma-Gilitanylitansferase A Chain)	B Chain B, Coagulation Factor Xiii (A-Subumit Zymogen) (E.C.2.3.2.13) (Protem- Glutamine Gamma-Glutamyltransferase A Chain)	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	B Chain B, Human Factor Xiii With Ytterbium Bound In The Ion Site	B Chain B, Human Factor Xiii With Strontium Bound In The Ion Site	A Chain A, Human Factor Xiii With Ytterbium Bound In The Ion Site	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	A Chain A, Human Factor Xiii With Strontium Bound In The Ion Site	similar to coagulation factor XIII, Al polypeptide	AF418272 1 coagulation factor XIII, A1 polypeptide	factor XIII a subunit	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	coagulation factor XIII A1 subunit precursor; Coagulation factor XIII, A polypeptide;	AAA52488.1 clotting factor XIIIa precursor (EC 2.3.2.13)	F13A HUMAN Coagulation factor XIII A chain precursor (Protein-glutamine gamma-	glutamyltransferase A chain) (Transglutaminase A chain)	protein-glutamine gamma-glutamyltransferase (EC 2.3.2.13), plasma	B Chain B, Recombinant Human Coagulation Factor Xiii	A Chain A, Recombinant Human Coagulation Factor Xiii
P58340	AAA99997.1	AAH07045.1	BAC04885,1	BAB71320.1	CAC36886.1	,	1F13	1F13	1GGT		ָרָבָּן בַּלָּבָּן	1GGU	1GGY	1QRK	1GGY	1GGU	1QRK	XP 165833.1	AAL12161.1	AAA52415.1	1EVU	1EVU	NP_000120.1	AAA52488.1	P00488	: N : N : N	EKHUX	1FIE	1FIE
3					F:(C-R)	10.2			;			:		,															
					Mm.17403 F:(C-IR)		·		-														1 }		13				
					NM_028784 NP_0830601		,										4								1 3				

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481 e-135	480 e-135	324 3E-88	3E-88	324 3E-88	324 3E-88	324 3E-88	324 3E-88	324 3E-88	3E-87	2E-86	7E-84	2E-81	2E-81	285 2E-76	1E-75	1E-75	1E-75	1E-75	1E-75	1E-75	1E-75	1E-75	7E-66	4E-64	244 4E-64	244 4E-64
481	480	324	324	324	324	324	324	324	321	318	310	301	301	285	283	283	283	283	283	283	283	283	250	244	244	244
factor XIII precursor	coagulation factor XIII, A1 polypeptide	high-mobility group box 1; high mobility group box 1; high-mobility group (nonhistone chromosomal) protein 1	HMG1 HUMAN High mobility group protein 1 (HMG-1)	nonhistone chromosomal protein HMG-1	HMG-1 protein (AA 1-215)	on-histone chromatin protein HMG1	AAH03378 high-mobility group (nonhistone chromosomal) protein 1	high-mobility group (nonhistone chromosomal) protein 1	HMG-1	nonhistone chromosomal protein HMG-1	dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)	HM1X_HUMAN High mobility group protein 1-like 10 (HMG-1L10)	bK445C9.3 (high-mobility group (nonhistone chromosomal) protein 1-like 10)	AC007277_1 similar to nonhistone chromosomal protein HMG-1 [Homo sapiens]; probable pseudogene; similar to P09429 (PID:g123369)	AAH00903 high-mobility group (nonhistone chromosomal) protein 2	high-mobility group box 2; high-mobility group (nonhistone chromosomal) protein 2	HMG2_HUMAN High mobility group protein 2 (HMG-2)	nonhistone chromosomal protein HMG-2	HMG-2	high mobility group 2 protein	AAH01063 high-mobility group (nonhistone chromosomal) protein 2	high mobility group protein 2	similar to dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)	high-mobility group box 3; high-mobility group (nonhistone chromosomal) protein 4	HMG4_HUMAN High mobility group protein 4 (HMG-4) (High mobility group protein 2a) (HMG-2a)	high mobility group protein 2a
AAA52489.1	AAH27963.1	NP_002119.1	P09429	S02826	CAA31110.1	AAB08987.1	AAH03378.1	AAH30981.1	BAA09924.1	S29857	CAB92731.1	Q9UGV6	CAB62951.1	AAF19244.1	AAH00903.2	NP_002120.1	P26583.	NSHUH2	- CAA44395.1	AAA58659.1	AAH01063.1	2001363A	XP_086648.2	NP_005333.1	015347	CAA71143.1
		F:(C-IR) -2				,					·				1			•					1			
		Mm.16421 F:(C-IR)			-														je same				1.2.2.		**	
	·	NM_010439 NP_034569.1																	energy of		: : : : : : : : : : : : : : : : : : : :					

Γ	1	- 1				
NM_013459 NP_038487.1	Mm.4407 F:(C-IR)		P00746	CFAD HUMAN Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	370	370 e-102
			CAC48304.1	adipsin/complement factor D precursor	358	358 4E-99
	٠		DBHU	complement factor D (BC 3.4.21.46) precursor [validated]	352	352 5E-97
		1	1FDP	A Chain A, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	34(340 IE-93
			1FDP	B Chain B, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	34(340 1E-93
			1FDP	D Chain D, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	34(340 IE-93
			1FDP	C Chain C, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	.34(340 1E-93
:	,		AAH34529.1	Unknown (protein for IMAGE:4780594)	34(340 1E-93
			1DST	Mutant Of Factor D With Enhanced Catalytic Activity	330	1E-90
·			1BIO	Human Complement Factor D In Complex With Isatoic Anhydride Inhibitor	329	4E-90
·	-		1DIC	A Chain A, Structure Of 3,4-Dichloroisocoumarin-Inhibited Factor D	375	329 4E-90
			1DSU	A Chain A, Human Factor D, Complement Activating Enzyme	325	329 4E-90
			1HFD	Human Complement Factor D In A P21 Crystal Form	325	329 4E-90
î			1DFP	A Chain A, Factor D Inhibited By Diisopropyl Fluorophosphate	325	329 4E-90
		· .	1DFP	B Chain B, Factor D Inhibited By Diisopropyl Fluorophosphate	329	4E-90
			1DSU	B Chain B, Human Factor D, Complement Activating Enzyme	326	329 4E-90
			XP_084037.1	similar to Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)		328 8E-90
	***		NP 001919.1	adipsin/complement factor D precursor	327	324 1E-88
3			AAA35527.1	adipsin/complement factor D	324	1E-88
AK017926	Mm.21697 F:(C-D) -	F:(C-D) -	NP_061931.1	RTP801	372	e-103
BAB31006.1		2.58				
			BAA91214.1	unnamed protein product	372	e-103
			AAH07714.1	hypothetical protein	37.	372 e-103
			AAH15236.1	hypothetical protein	372	372 e-103
î.			AAL38424.1	RTP801	372	372 e-103
			AAM10442.1	REDD-1	372	372 e-103
			CAB66603.1	hypothetical protein	370	370 e-102

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364 e-100	364 e-100	364 e-100	e-100	364 e-100	364 e-100	361 e-100	360 3E-99	359 4E-99	350 3E-96	317 e-136		e-136	e-136	e-135	313 e-135	0		0	0	0	0	. 0	0	0	0_
364	364	364	364	364	364	361	360	359	350	317	· ·	317	317	313	313	1196 0		1196 0	119610	1196 0	11960	1196	1195	1195 0	1023 0
suppressor of cytokine signaling-2; STAT induced STAT inhibitor-2; cytokine-inducible SH2 protein 2	similar to Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	SOC2_HUMAN Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	STAT induced STAT inhibitor-2	STAT-induced STAT inhibitor-2	STAT induced STAT inhibitor-2	STAT induced STAT inhibitor 2	cytokine-inducible SH2 protein 2	CIS2	suppressor of cytokine signalling-2; HSSOCS-2	unknown		similar to SET domain and mariner transposase fusion gene	Similar to SET domain and mariner transposase fusion gene	SET domain and mariner transposase fusion gene	orf; encodes putative chimeric protein with SET domain in N-terminus with similarity to several other human, Drosophila, nematode and yeast proteins	transferrin receptor (p90, CD71); Transferrin receptor		TFR1_HUMAN Transferrin receptor protein 1 (TR1) (TR) (TR) (Trft) (CD71 antigen)	fransferrin recentor	put. transferrin receptor (aa 1-760)	transferrin receptor	transferrin receptor	AF187320 1 transferrin receptor	AAH01188 transferrin receptor (p90, CD71)	C Chain C, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor
NP_003868.1	XP_170547.1	014508	BAA22429.1	AAC34745.1	AAH10399.1	JC5626	JC5760	BAA22536.1	AAC98896.1	AAC09350.1		XP 057054.6	AAH11635.1	NP 006506.1	AAC52012.1	NP_003225.1		P02786	IXHII	CAA25527.1	AAA61,153.1	1011297A	AAF04564.1	AAH01188.1	1DE4
F:(C-D) - 2.03	. 1					\ \ \ !					2.02		41				2.02								
Mm.4132 F:(C.D) - NP 2.03										Mm.56539			1			Mm.26069									
NM_007706 NP_031732.1					,					AK017895	XP 132692.1	÷	,			NM_011638	NP_035768.1						4.00		X - 1

28	224 6E-58	77.7	XP_165392.1 similar to folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	XP_165392.1			
65	228 3E-59	228	AAM34479.1 prostate-specific membrane antigen	AAM34479.1			
59	228 3E-59	228	AF176574 1 folylpoly-gamma-glutamate carboxypeptidase	AAD51121.1		٠. ن	:
59	228 3E-59	228	_	AAÁ60209.1		1 1 4 5 kg	
59	228 3E-59	228	prostate-specific membrane antigen	A56881	*1 1	• • •	. \$3
			gluialinaté carooxypépindasé) (FUCF) (Folaté nydrolasé 1) (Frostaté-spécific mémbrané antigén) (PSMA) (PSM)				
•			(NAALADase I) (Pteroylpoly-gamma-glutamate carboxypeptidase) (Folylpoly-gamma-	- 4			. :
66	228 3E-59	228	FOH1_HUMAN Glutamate carboxypeptidase II (Membrane glutamate carboxypeptidase) (mGCP) (N-acetylated-alpha-linked acidic dipeptidase I)	Q04609			1
66	228 3E-59	228	folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	NP_004467.1		•	
29	228 2E-59	228	prostate-specific membrane antigen	AAC83972.1			
35	5 2E-85	315	unnamed protein product	BAA91153.1	:		1
	498 e-140	498	transferrin-receptor2	AAC78796.1			;
13 	498 e-140	498	transferrin receptor 2	NP 003218.1	;	¢.	
4	545 e-154	545	AF067864 1 transferrin receptor 2 alpha	AAD45561.1			
4	545 e-154	545	TFR2_HUMAN Transferrin receptor protein 2 (TfR2)	Q9UP52		,	
	0	1020	H Chain H, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			• 1
	0	1020 0	G Chain G, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
	<u>0</u>	1020 0	F Chain F, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
Γ	0	1020 0	E Chain E, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
	0	1020	D Chain D, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8		·	
	0 (1020 0	C Chain C, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8	·		
Γ	0	1020	B Chain B, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
Γ	ြ	1020	A Chain A, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8		:	;
Π	0	1023 0	I Chain I, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor	1DE4			
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100 100	0	C	0		623 e-178	619 e-177	594 e-169	575 e-164	541 e-153	541 e-153	450 e-126	340 5e-93	0	0	0
	835	786	745	623	623	619	594	575	541	541	450	340	765	759	753
iliferenigally ampressedeling etter nord die se iner typensie. In er in er ein ein eine in ein eine ingen	60kDa BRG-1/Brm associated factor subunit c isoform 2	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d3; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60C; Swp73-like protein; chromatin remodeling complex BAF60C subunit; SWI/SNF complex 60 kDa subunit C		SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1 isoform a; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A	SMARCD1 protein	SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin D1	SWI/SNF-related matrix-associated actin-dependent regulator ofchromatin d2; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60B; Swp73-like protein; chromatin remodeling complex BAF60B subunit; SWI/SNF complex 60 kDa subunit B	SWI/SNF complex 60 KDa subunit	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1 isoform b; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A	SWI/SNF complex 60 KDa subunit	unknown	unknown	1 alpha 1 actin precursor; alpha skeletal muscle actin	1 cardiac muscle alpha actin proprotein; smooth muscle actin	1 alpha 2 actin; alpha-cardiac actin
in in the second	AAR88510.1	UP 003069.2	AC50697.1	VP_003067.2	\AH09368.2	\AD23390.1	NP_003068.2	AAC50696.1	NP_620710.1	4AC50695.1	AAS02031.1	\AS00380.1	NP_001091.1	NP_005150.1	NP_001604.1
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15/08239	8					1	37_									PC	1/(J S Z(JUS,	/00:	5590	b			
389 e-108	385 e-106	384 e-106	380 e-105	366 e-101	366 e-101	363 e-100	362 e-100	362 1e-99	361 2e-99	359 6e-99	358 2e-98	332 7e-91	331 2e-90	323 4e-88	321 2e-87	321 2e-87	321 2e-87	310 36-84	310 5e-84	300 3e-81	299 9e-81	299 9e-81	1	765 0	762 0
ARM1_HUMA N Actin related protein M1	NP_115876.2 actin related protein M1	AAH07289.1 Actin related protein M1	CAA57692.1 beta-centractin	NP_612146.1 actin-related protein T1	AAM00432.1 actin-related protein T1	NP_536356.3 actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	AAP20055.1 HSD27	BAB85862.1 actin-related protein hArpM2	NP_005713.1 actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	AAH29499.1 Actin-related protein M2	AAH14546.1 Actin-related protein 2	AAP37280.1 actin alpha 1 skeletal muscle protein		XP_377904.1 similar to cytoplasmic beta-actin	AAH36253.1 ACTR2 protein	AAH10417.2 ACTG1 protein	NP_006678.1 actin-like 7A; actin-like 7-alpha	NP_006677.1 actin-like 7B; actin-like 7-beta	AAH09544.1 Unknown (protein for IMAGE:3897065)	NP_848620.1 actin-like	AAP20052.1 HSD21	XP_377631.1 similar to beta actin	Mm.213025 F:(C-D)	-1.53 NP_001604.1	ATHUSM actin alpha 2, aortic smooth muscle
																							7392	1418.1	

NP_005150.1 car	cardiac muscle alpha actin proprotein; smooth muscle actin	755	-0
NP_001606.1 act	actin, gamma 2 propeptide; actin, alpha-3	754	0
NP_001091.1 alp	alpha 1 actin precursor; alpha skeletal muscle actin	. 753	0
ND 00460E 4 26	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant	· ·	
	zo, dealless, addosolital dollillatt zo,	124	5
	gamma-actin	724	0
NP_001092.1 bet	beta actin; beta cytoskeletal actin	724	0
AAH16045.1 Be	Beta actin	722	0
CAA45026.1 mu	mutant beta-actin (beta'-actin)	720	<u></u>
AAH08633.1 act	actin, beta	719	0
AAH12854.1 AC	ACTB protein	703	0
AAH17450.1 Un	Unknown (protein for IMAGE:3538275)	701	0
XP_293924.1 sim	similar to RIKEN cDNA 4732495G21 gene	689	0
XP_371558,2 sin	similar to FKSG30	210	0
XP_065237.5 sir	similar to FKSG30	671	0
AAG50355.1 FK	FKSG30	671	0
XP_292982.4 sin	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	899	0
XP_372957.1 sin	similar to FKSG30	899	0
AAA51586.1 act	actin prepeptide	661	0
0902248A			
act	actin beta related pseudogene	575 e-163	163
AAH23548.1 AC	ACTG1 protein	506 e-143	143
AAA51580.1 gar	gamma-actin	445 e-124	124
AAH06372.1 AR	ARP1 actin-related protein 1 homolog B, centractin beta	431 e	e-120
` .	ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast		
NP_005/26.1 nor	nomoiog is	429 e-120	-120
AR	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV;		
7.1	centrosome-associated actin homolog; ARP1, yeast homolog	422 e-118	118
•••	actin-related protein	421 e-117	117
ARM1_HUMA N Act	Actin related protein M1	387 e-107	107
		3	<u>-</u>

		•		
	NP_115876.2	actin related protein M1		382 e-105
	AAH07289.1	Actin related protein M1		382 e-105
	CAA57692.1	beta-centractin	•	380 e-105
,	NP 612146.1	actin-related protein T1	:	369 e-102
	AAM00432.1	actin-related protein T1		369 e-102
	NP_536356.3	actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	42; actin-related protein T2	369 e-102
	BAB85862.1	actin-related protein hArpM2		367 e-101
	AAP20055.1	HSD27	,	366 e-101
	AAH29499.1	Actin-related protein M2		365 e-100
	NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	2, yeast) homolog	356 6e-98
	AAH14546.1	Actin-related protein 2		353 5e-97
•	NP_006678.1	actin-like 7A; actin-like 7-alpha		328 2e-89
	XP_208204.1	similar to actin-related protein 2		326 7e-89
	XP_377904.1	similar to cytoplasmic beta-actin		325 2e-88
•	AAP37280.1	actin alpha 1 skeletal muscle protein		323 6e-88
	AAH10417.2	ACTG1 protein	=	323 8e-88
	AAH36253.1	ACTR2 protein		318 16-86
	NP_006677.1	actin-like 7B; actin-like 7-beta		316 9e-86
	AAH09544.1	Unknown (protein for IMAGE:3897065)	• •	311 2e-84
	BAB71690.1	unnamed protein product		303 6e-82
	NP_848620.1	actin-like	•	303 8e-82
•	AAP20052.1	HSD21		301 2e-81
013456 F:(C-E	· (c		. '	168
038484.1 Mm.5316 -1.46 I	NP_001095.1	skeletal muscle specific actinin, alpha 3		5
•				144
	NP_001094.1	NP_001094.1 actinin, alpha 2		0
				141
	NP_001093.1	actinin, alpha 1		0
,				140
	FAHUAA	alpha-actinin 1 - human		0 2
				134
	NP_004915.2	actinin, alpha 4	•	. 0 8 :

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924 . 0
899
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753 0
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497 e-140
426 e-118
426 e-118
415 e-115
405 e-112
405 e-112
405 e-112
399 e-110
399 e-110
399 e-110 399 e-110
396 e-110
396 e-110

	BAA83821.1	actin binding protein ABP620	224 8e-58
		microfilament and actin filament cross-linker protein isoform a; 620 kDa actin binding protein; actin cross-linking factor; macrophin 1; trabeculin-alpha; actin	
-	NP_036222.3	cross-linking family protein 7	224 8e-58
	AAF06360.1	trabeculin-alpha	223 2e-57
	S66292	actin-crosslinking protein ACF7 - human (fragment)	215 3e-55
	1MB8_A	Chain A, Crystal Structure Of The Actin Binding Domain Of Plectin	211 7e-54
	CAA60503.1	alpha-spectrin	203 1e-51
NM_026369 F:(C-D)			
NP_080645.1 Mm.288974 -1.38	NP_005708.1	actin related protein 2/3 complex subunit 5; Arp2/3 protein complex subunit p16	293 8e-79
	AAH57237.1	ARPC5 protein	285 1e-76
	AAP97155.1	ARC16-2	211 4e-54
	NP_112240.1	actin related protein 2/3 complex, subunit 5-like	210 5e-54
NM_018817 F:(C-D)	;	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121
NP_061287.1 Mm,274232 -1.37	NP_054859.2	1; HepA-related protein; SMARCA-like protein 1	3
	÷ 1	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121
	AAH16482.1		0
			120
	AAF24984.1	HepA-related protein HARP	0
	.: '. .i		112
	T34557	hypothetical protein DKFZp434B1050.1 - human (fragment)	2
	BAA90955.1	unnamed protein product	975
	BAC04536.1	unnamed protein product	220 1e-56
NM 026552 F.(C-D)			
1 Mm.289306	"NP_005709.1	actin related protein 2/3 complex subunit 4; Arp2/3 protein complex subunit p20	326 5e-89
	AAH12596.2	ARPC4 protein	322 1e-87
AF316037 F:(C-D)		actin-binding LIM protein 1 isoform a; LIM actin-binding protein 1; limatin;	130
NP_848803.2 Mm.244618 -1.35 NP_	NP_002304.2	actin-binding LIM protein	_
			130
	AAC51676.1	actin-binding double-zinc-finger protein	:
			127
	BAA06681.2 KIAA0059	KIAA0059	2.

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actin-binding LIM protein 1 isoform m; LIM actin-binding protein 1; limatin; actin-binding LIM protein			KIAA0843 protein	actin binding LIM protein family, member 3	Unknown (protein for IMAGE:6188753)	KIAA1808 protein	actin binding LIM protein family, member 2	unnamed protein product	ABLIM1 protein	ABLIM3 protein	uncharacterized hypothalamus protein HARP11		unnamed protein product	unnamed protein product	unnamed protein product	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV; centrosome-associated actin homolog; ARP1, yeast homolog	actin-related protein	•	•,	ARP1 actin-related protein 1 homolog B, centractin beta	beta-centractin	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 26; deafness, autosomal dominant 20;	gamma-actin	l cardiac muscle alpha actin proprotein; smooth muscle actin	beta actin; beta cytoskeletal actin
NP_006710.2		NP_006711.2	BAA74866.2	NP_055760.1	AAH67214.1	BAB47437.1	NP_115808.2	BAC04414.1	AAH02448.1	AAH01665.1	D) NP 060947.1	BAA	BAB14083.1	CAD62610.1	CAD61940.1	D) NP_005727.1	1818358A		NP_005/26.1	AAH06372.1	CAA57692.1	NP_001605.1	JC5818	NP_005150.1	NP_001092.1
											NM_019785 F:(C-D) NP_062759.1 Mm_29317 -1.32					NM_016860 F:(C-D) NP_058556.1 Mm.3118 -1.31									

424 e-118	424 e-118	423 e-118	423 e-118	422 e-117	422 e-117	422 e-117	417 e-116	410 e-114	408 e-113	408 e-113	408 e-113	404 e-112	404 e-112	404 e-112	355 2e-97		330 6e-90	322 2e-87	318 2e-86	314 6e-85	· .	314 6e-85	309 1e-83	309 2e-83	308 2e-83	307 7e-83	297 6e-80	296 1e-79	295 4e-79
		•	1 .			•						1	stis, and placenta					east) homolog				1	actin-related protein Ta			<u> </u>			-
	-		letal muscle actin		alpha-3	9	321 gene	3275)					in prostate, ovary, tes	•			1	in-related protein 2, ye					ated protein hArpM2; a	Ī				•	
actin, beta	Beta actin	nutant beta-actin (beta'-actin)	alpha 1 actin precursor; alpha skeletal muscle actin	alpha 2 actin; alpha-cardiac actin	actin, gamma 2 propeptide; actin, alpha-3	actin alpha 2, aortic smooth muscle	similar to RIKEN cDNA 4732495G21 gene	Unknown (protein for IMAGE:3538275)	ACTB protein	FKSG30	similar to FKSG30	similar to FKSG30	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	similar to FKSG30	actin prepeptide		actin beta related pseudogene	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	Actin-related protein 2	actin related protein M1		Actin related protein M1	actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	Actin related protein M1	actin-related protein hArpM2	Actin-related protein M2	ACTG1 protein	similar to actin-related protein 2	actin-related protein T1
AAH08633.1 ad		CAA45026.1 m	NP_001091.1 al	NP_001604.1 al	NP_001606.1 ad	ATHUSM a	XP_293924.1 si	AAH17450.1 U	AAH12854.1 A	AAG50355.1 F	XP_065237.5 si	-		XP_372957.1 si	:	0902248A	 	NP_005713.1 a	AAH14546.1 A	NP_115876.2 a	_	-	NP_536356.3 a	AAH07289.1 A	BAB85862.1 a	AAH29499.1 A	AAH23548.1 A	XP_208204.1 s	NP_612146.1 a

Coronin 2B (Coronin-like protein C) (ClipinC) (Protein FC96)

	235 3e-61 213 1e-54 203 1e-51	-170	00	0. 0	0	4 4
	8 2 8	597 e-170 594 e-169	954 946	758	644	412 e-114 411 e-114
actin-related protein T1 HSD27 ACTR2 protein actin-like 7A; actin-like 7-alpha actin-like 7B; actin-like 7-beta gamma-actin unnamed protein product actin-like HSD21 actin-related protein 3-beta; actin-related protein 3-beta; actin-related protein Arp11 ARP3 actin-related protein 3 homolog; ARP3 (actin-related protein 3, yeast)		SWI/SNF-related matrix-associated actin-dependent regulator of chromatin e1; mammalian chromatin remodeling complex BRG1-associated factor 57 SWI/SNF-related matrix-associated actin-dependent regulator of chromatin e1	hypothetical protein DKFZp762H186.1 - human (fragment) coronin, actin binding protein, 1C; coronin, actin-binding protein, 1C; coronin, actin-binding protein, 1C;	coronin, actin binding protein, 1B coronin, actin-binding, 1A; coronin, actin-binding protein, 1A; coronin, actin-binding protein, 1A; coronin-1		KIAA0925 protein coronin, actin binding protein, 2B; clipin C; coronin, actin-binding, 2B; coronin, actin-binding protein, 2B
AAM00432.1 AAH36253.1 NP_006678.1 NP_006677.1 AAA51580.1 BAB71690.1 NP_848620.1 AAP20052.1 AAP20052.1		NM_020618 F:(C-D) NP_065643.1 Mm.27330 -1.30 NP_003070.3 AAH07082.1 NM_011779 F-(C-D)	NP_035909.2 Mm.320560 -1.30 T47172 NP_055140.1	NP_065174.1 NP_065174.1	AAA77058.1	BAA76769.1 NP 006082.1

	NP_438171.1	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein 2; WD protein IR10	408 e-113
	NP_003380.2	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein2; WD protein IR10	408 e-113
	AAB47807.1	WD protein IR10	404 e-112
	T47174	hypothetical protein DKFZp7621166.1 - human (fragment)	389 e-107
	AAS48630.1	unknown	314 7e-85
	NP_116243.1	hypothetical protein FLJ14871	311 5e-84
	AAQ04659.1	Unknown	311 6e-84
	NP_078811.1	hypothetical protein FLJ22021	234 6e-61
M_033268 F:(C-D)			171
2.1505/1.2 IMM.195067	N001094	actinin, alpna z	7 7
	NP_001095.1	skeletal muscle specific actinin, alpha 3	141
*	NP 0010931	actinin alnha 1	139
			t 05
	FAHUAA	alpha-actinin 1 - human	<u>-</u>
	NP 004915.2	actinin albha 4	136
			- 36
:	BAA24447.1	alpha actinin 4	
			126
,	AAC17470.1	alpha actinin	ಬ
	AAH15620.2	ACTN4 protein	941
	1HCI_A	Chain A, Crystal Structure Of The Rod Domain Of Alpha-Actinin	891
•	1HCI_B	Chain B, Crystal Structure Of The Rod Domain Of Alpha-Actinin	891
	CAA38970.1	alpha-actinin	887
	CAD62344.1	unnamed protein product	835
	XP 2936694	similar to actinin alpha 4	521 o 118

455 e-127 412 e-114 ic-1 408 e-113	ic-1 407 e-113 in, beta, 391 e-108	391 e-108	391 e-108	381 e-105	:	381 e-105	381 e-105	375 e-103	375 e-103	373 e-103		284 5e-76	284 5e-76	279 2e-74	231 5e-60	
Chain A, Crystal Structure Of Two Central Spectrin-Like Repeats From 1QUU_A Alpha-Actinin NP_008877.1 spectrin, beta, non-erythrocytic 2 spectrin, beta, non-erythrocytic 1 isoform 2; Spectrin, beta, nonerythrocytic-1	spectrin, beta, non-erythrocytic 1 isoform 1; Spectrin, beta, nonerythrocytic-1 NP_003119.1 (beta-fodrin) spectrin, beta, erythrocytic (includes spherocytosis, clinical type I); Spectrin, beta, NP_000338.2 erythrocytic; spectrin, beta, erythrocytic (includes sperocytosis, clinical type I)	SPCB_HUMA N Spectrin beta chain, erythrocyte (Beta-I spectrin)	AAA60578.1 spectrin Rouen (beta-220-218) mutant coding sequence	AAG42473.1 spectrin beta IV	NP_066022.1 spectrin, beta, non-erythrocytic 4 SPCQ_HUMA Spectrin beta chain 3)(Beta-IV	N spectrin)	AAQ14859.1 beta spectrin IV	NP_079489.1 spectrin, beta, non-erythrocytic 4	AAF93171.1 betalV spectrin isoform sigma2	AAF93173.1 betaIV spectrin isoform sigma4	NP_057726.1 spectrin, beta, non-erythrocytic 5; beta V spectrin	AAB41498.1 alpha II spectrin	AAH53521.1 SPTAN1 protein	NP_003118.1 spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	CAA60503.1 alpha-spectrin	

224 6e-58	224 8e-58	223 1e-57	223 1e-57	223 1e-57	223 1e-57	223 16-57	223 1e-57	223 16-57	222 2e-57	222 2e-57	220 1e-56	219 2e-56		213 1e-54	1e-54	213 1e-54	211 7e-54
224	224	223	223	223	223	523	223	223	. 222	222	220			213	213	23	211
plectin 1 isoform 2; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958780.1 (Ogna)	plectin 1 isoform 8; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958784.1 (Ogna)	plectin 1 isoform 11; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958786.1 (Ogna)	plectin 1 isoform 6; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958782.1 (Ogna)	plectin 1 isoform 10; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958785.1 (Ogna)	plectin 1 isoform 7; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958783.1 (Ogna)	plectin 1 isoform 1; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_000436.2 (Ogna)	G02520 plectin - human	plectin 1 isoform 3; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958781.1 (Ogna)	bullous pemphigoid antigen 1 isoform 1; bullous pemphigoid antigen 1 NP_899236.1 (230/240kD); dystonin; hemidesmosomal plaque protein	l39160 dystonin isoform 1 - human (fragment)	PLE1_HUMA N Plectin 1 (PLTN) (PCN) (Hemidesmosomal protein 1) (HD1)	BPA1_HUMA Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid N antigen) (BPA) (Hemidesmosomal plaque protein) (Dystonia musculorum protein)	MACE UI MA protoin 7) (Macrophin 4) (Trabonilio alcho) (2011) (2012)	N	BAA83821.1 actin binding protein ABP620	NP_036222.3 cross-linking family protein 7	AAF06360.1 trabeculin-alpha

SPCA_HUMA N	১ Spectrin alpha chain, erythrocyte (Erythroid alpha-spectrin)	210 16-53
S66292	actin-crosslinking protein ACF7 - human (fragment)	209 2e-53
F:(C-D) Mm.183102 -1.23 NP_005712.1	ARP3 actin-related protein 3 homolog; ARP3 (actin-related protein 3, yeast) I homolog	850 0
NP_065178.1	actin-related protein 3-beta; actin-related protein 3-beta; actin-related protein Ap11; actin-related protein Ap11	793 0
AAP97150.1	actin related protein ARP4	662 0
AAH15207.1	ARP3BETA protein	597 e-170
XP_374583.1	l similar to actin-related protein Arp11	348 3e-95
JC7580	actin-related protein Arp11 - human	344 4e-94
AAK31778.1	FKSG74	253 8e-67
AAK31776.1	FKSG72	252 2e-66
AAK31777.1	FKSG73	249 2e-65
AAH16045.1	Beta actin	248 3e-65
NP_001092.1	l beta actin; beta cytoskeletal actin	248 3e-65
NP_001605.1	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant 1 26; deafness, autosomal dominant 20; cytoskeletal gamma-actin	248 4e-65
JC5818	•	248 4e-65
NP_001091.1	1 alpha 1 actin precursor; alpha skeletal muscle actin	248 5e-65
CAA45026.1	mutant beta-actin (beta'-actin)	247 6e-65
AAH08633.1	actin, beta	247 8e-65
NP_005150.1	cardiac muscle alpha actin proprotein; smooth muscle actin	247 8e-65
XP_293924.1	I similar to RIKEN cDNA 4732495G21 gene	246 1e-64
ATHUSM	actin alpha 2, aortic smooth muscle - human	246 1e-64
NP_001604.1	1 alpha 2 actin; alpha-cardiac actin	246 2e-64
NP_001606.1	1 actin, gamma 2 propeptide; actin, alpha-3	245 3e-64
AAH17450.1	nknown (protein for IMAGE:3538275)	239 2e-62
	ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1	
NP 005726.1	(acuit related protein 1, yeast) nomorog 5 (centracun beta); PCS, ARP1, yeast 1 homolog B	236 1e-61
1		1.,

589 e-168	SMARCD1 protein	AAH09368.2		
596 e-170	SWI/SNF complex 60 KDa subunit	AAC50697.1		
619 e-177	60kDa BRG-1/Brm associated factor subunit c isoform 2	AAR88510.1		
622 e-178	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d3; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60C; Swp73-like protein; chromatin remodeling complex BAF60C subunit; SWI/SNF complex 60 kDa subunit C	NP_003069.2		
745 0		AAC50696.1		
828 0		F:(C-D) -1.21 NP_003068.2	F:((VM_031878 VP_114084.1 Mm.21772
		NP_005713.1		
202 40 54		AAH14546.1		
	1 actin prepentide	CAA51586.1		
223 2e-57	ุณ	XP_371558.2		
	.4 similar to pote protein; Expressed in prostate, ovary, testis, and placenta	XP_292982.4		
		AAG50355.1		
223 1e-57	,	XP_065237.5		
	1 ARP1 actin-related protein 1 homolog B, centractin beta	AAH06372.1 XD 372067.1		
234 46-61		1818358A		
235 3e-61	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV; 1 centrosome associated actin homolog; ARP1, yeast homolog A	NP_005727.1		
236 2e-61	:	AAH12854.1		

SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1 doff actor 604; chromatin remodeling complex BRG1-associated factor 604; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin D1 SWI/SNF-related matrix-associated actin-dependent regulator of chromatin D1 SWI/SNF-related matrix-associated actin-dependent regulator of chromatin D1 SWI/SNF complex BSC50; mammalian chromatin remodeling complex BRG1-associated factor 604; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A AAS00331.1 unknown AAS00330.1 sWI/SNF complex 60 kDa subunit A AAS00330.1 unknown AAF20280.1 actin related protein 2/3 complex subunit 1A, SOP2-like protein AF140280.1 actin related protein 2/3 complex subunit 1B; AR22/3 protein complex subunit AAF10280.1 actin related protein 2/3 complex subunit 1B; AR22/3 protein complex subunit NP_005711.1 p41; actin related protein 2/3 complex subunit 1A (41 kD) actin-related protein 2/3 complex subunit 1B; AR22/3 protein complex subunit NP_003084.1 unknown SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1; sucrose nonfermenting, yeast, homolog-like 1; integrase siteractor 1 protein) (15NF5) (BAF47) CAA09789.1 Initb BAB14784.1 unnamed protein product CAA08789.1 Initb BAB14784.1 unnamed protein		romatin d1 1-associated 1-like protein; 589 e-168 ihromatin D1 582 e-165 iromatin d1 1-associated 1-like protein; 505 e-142	505 e-142	366 e-100	201 56-59 159 2e-38	152 2e-36	730 0	723 0	533 e-15		hromatin, e 1: integrase	754 0	rromatin 749 0	!		
NP_003067.2 AAD23390.1 AAD23390.1 AAC50695.1 AAS00380.1 AAS00380.1 AAF20280.1 AAF20280.1 AAF20280.1 NP_006400.2 AR1A_HUMA N NP_003064.2 SNF5_HUMA N CAA09759.1 CAA09759.1 CAA09759.1	NP_003067.2 AAD23390.1 NP_620710.1 AAS02380.1 AAS02380.1 AAS0380.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20381.1 AAF1A_HUMA N CAA09759.1 BAB14784.1 CAA76639.1	tin-dependent regulator of ct lin remodeling complex BRG olex BAF60A subunit, Swp73 ctin-dependent regulator of ct tin-dependent regulator of ct in remodeling complex BRG olex BAF60A subunit; Swp73					nit 1A; actin binding protein (e); SOP2-like protein	nit 1A (SOP2-like protein)	iit 1B; ARP2/3 protein compl subunit 1A (41 kD)		tin dependent regulator of commenting, yeast, homolog-like		tin dependent regulator of clastor of clastor 1 protein) (hSNF5) (BA			
NP_003067.2 AAD23390.1 AAD23390.1 AAC50695.1 AAS00380.1 AAS00380.1 AAF20280.1 AAF20280.1 AAF20280.1 NP_006400.2 AR1A_HUMA N NP_003064.2 SNF5_HUMA N CAA09759.1 CAA09759.1 CAA09759.1	NP_003067.2 AAD23390.1 NP_620710.1 AAS02380.1 AAS02380.1 AAS0380.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20280.1 AAF20381.1 AAF1A_HUMA N CAA09759.1 BAB14784.1 CAA76639.1	lated matrix-associated ac sc6p; mammalian chromat thromatin remodeling comp implex 60 kDa subunit A lated, matrix-associated, a lated matrix-associated act sc6p; mammalian chromat thromatin remodeling comp mplex 60 kDa subunit A	mplex 60 KDa subunit		rotein		protein 2/3 complex subun naromyces pombe sop2-lik	protein 2/3 complex subur	protein 2/3 complex subun lated protein 2/3 complex,		ated, matrix associated, acmember 1; sucrose nonfer		ated <u>,</u> matrix associated, ac nember 1 (Integrase intera		otein product	rotein
	F.(C-D) 1.14 L			•		PR02451		_		unknown				٠.		
		NP_003067 AAD23390.1 NP_620710.	AAC50695.1	AAS00380.1	AAH18953.2) NP_006400.	AR1A_HUM.	NP_005711.	AAS00381.1	(6	NP_003064	NOT CHOM	CAA09759.1	BAB14784.1	CAA76639.1

WO 2005/082398 PCT/US2005/005596

Subtable 1B: Wholly Unfavorable Genes and Proteins

Unigene Behavior Human Protein Name Mm.4642 3.8 Proteins BAA86929.1 calcitonin receptor Mm.4642 3.8 BAA86929.1 calcitonin receptor BAA86929.1 calcitonin receptor CAA49541.1 Inman calcitonin receptor CAA57849.1 tuncated isomer of calcitonin receptor CAA57849.1 tuncated isomer of calcitonin receptor AAB83945.1 Calcitonin Receptor, alternatively spliced form AAA85640.1 calcitonin receptor AAA35640.1 calcitonin receptor AAA35640.1 calcitonin receptor AAA5540.1 calcitonin receptor CARE HUMAN Calcitonin receptor AAA5540.1 calcitonin receptor AAA55640.1 AAA5560.1 calcitonin receptor AAA5560.1 calcitonin receptor site material spliced form AAA6200.1 calcitonin receptor site protein AAA62158.1 calcitonin receptor like protein AAA62158.1 <td< th=""><th>_</th><th></th><th></th><th></th><th></th><th></th></td<>	_					
U:(IR-D) 3.8 BAA86929.1 BAA86929.1 BAA86929.1 BAA86928.1 IBT217 CAA49541.1 CAA49541.1 CAA49541.1 AAB83945.1 AAB83947.1 AAA835640.1 AAA83944.1 AAA83944.1 AAA8256301.1 NP_005786.1 ICZ477 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1	61.5			Human Protein Name	Score (bits)	E-value
3.8 AAC50300.1 BAA86929.1 BAA86928.1 NP 001733.1 I37217 CAA49541.1 CAA49541.1 CAA57849.1 AAB83945.1 AAB83945.1 AAB83944.1 AAC50301.1 NP 005786.1 IC2477 AAA62158.1 AAC41994.1 AAC41994.1 NP 000307.1 O03431	•	U:(IR-D)				
BAA86929.1 BAA86928.1 NP 001733.1 I37217 CAA49541.1 CAA57849.1 AAB83945.1 AAB83944.1 AAA35640.1 AAA35640.1 AAA62158.1 AAA62158.1 AAA62158.1 AAC41994.1 NP 000307.1 NP 0003431 A49191	54		AAC50300.1	calcitonin receptor	758	0
BAA86928.1 NP 001733.1 137217 CAA49541.1 CAA57849.1 AAB83945.1 P30988 S34486 AAB83944.1 AAC50301.1 NP_005786.1 Q16602 JC2477 AAA62158.1 AAC41994.1 AAC41994.1 NP_000307.1 Q03431 A49191	1	i i	BAA86929.1	calcitonin receptor	758	0
NP 001733.1 137217 CAA49541.1 CAA57849.1 AAB83945.1 P30988 S34486 AAA35640.1 AAA35640.1 AAA35640.1 AAA35640.1 AAA35640.1 AAA4558.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1 AAA62158.1	1		BAA86928.1	calcitonin receptór	758	0
741.1 749.1 740.1 740.1 786.1 786.1 194.1 994.1	. [, j	,	calcitonin receptor	754	0
741.1 745.1 745.1 740.1 744.1 786.1 786.1 786.1 786.1				calcitonin receptor	754	Ó
749.1 745.1 740.1 786.1 786.1 786.1 786.1 786.1			CAA49541.1	human calcitonin receptor	754	0
745.1 740.1 744.1 786.1 786.1 786.1 786.1 394.1			CÀA57849.1	truncated isomer of calcitonin receptor	754	0
540.1 144.1 101.1 786.1 786.1 158.1 194.1		,	AAB83945.1	Calcitonin Receptor, alternatively spliced form	754	0
740.1 744.1 786.1 786.1 786.1 786.1 394.1			P30988	CALR_HUMAN Calcitonin receptor precursor (CT-R)	748	0
640.1 301.1 7786.1 158.1 1994.1 307.1			S34486	calcitonin receptor	748	0
944.1 301.1 786.1 158.1 994.1 307.1			AAA35640.1	calcitonin receptor	748	0
301.1 7786.1 158.1 158.1 307.1	•		AAB83944.1	Calcitonin Receptor, alternatively spliced form	744	0
786.1	٠. ا		AAC50301.1	calcitonin receptor isoform	731	0
158.1 994.1 307.1				calcitonin receptor-like	511	e-144
158.1 994.1 1307.1	:		Q16602	CGRR_HUMAN Calcitonin gene-related peptide type 1 receptor precursor (CGRP type 1 receptor)	511	e-144
62158.1 41994.1 000307.1 31 91	ı	·	JC2477	calcitonin receptor-like protein	511	e-144
41994.1 000307.1 31 91	`		AAA62158.1	calcitonin-like receptor	511	e-144
31 91	ı		AAC41994.1	CGRP type 1 receptor	511	e-144
31	•			parathyroid hormone receptor 1	237	1e-61
91			Q03431	PTRR_HUMAN Parathyroid hormone/parathyroid hormone-related peptide receptor precursor (PTH/PTHR receptor)	237	1e-61
	ļ		A49191	parathyroid hormone/PTH-related peptide receptor	237	

,			AAA36525.1	parathyroid hormone receptor	237	1e-61
,	,		CAA48589.1	parathyroid hormone receptor	237	1e-61
		:	AAA56774.1	parathyroid hormone/parathyroid hormone related peptide receptor	. 237	1e-61
		; ;	AAB60657.1	parathyroid hormone/PTH-related peptide receptor	237	1e-61
	•		2119172A	parathyrin receptor	237	1e-61
ì			Q13324	CRF2_HUMAN Corticotropin releasing factor receptor 2 precursor (CRF-R 2) (CRF2) (Corticotropin-releasing hormone receptor 2) (CRH-R 2)	221	6e-57
			AAC71653.1	corticotropin-releasing factor receptor	221	6e-57
; ·			BAC05922.1	seven transmembrane helix receptor	221	6e-57
7			AAB94503.1	corticotropin releasing hormone receptor type 2 beta isofor	221	8e-57
			AAB94562.1	corticotropin releasing hormone receptor type 2 gamma isoform; CRH type 2 gamma receptor	220	1e-56
			AAC71654.1	corticotropin releasing hormone receptor type 2 gamma isoform; match to AF019381 (PID:g2738889)	220	1e-56
AK007657						
		U:(IR-D)	-			
BAB25167.1	Mm.45138	3.55	NP 115744.2	15744.2 leucine zipper and CTNNBIP1 domain containing	305	9e-83
			BAB72100.1	Leucine zipper & ICAT homologous protein LZIC	305	9e-83
AK007999	:				•	
BAB25399.1	U:(Mm.35718 3.3	U:(IR-D) 3.3	XP_114275.1	similar to RIKEN cDNA 2010001C09	244	1e-64
AF282730 AAF97239.1	Mm.36851	U:(IR-D) 2.78	NP 003247.1	tissue inhibitor of metalloproteinase 4 precursor	409	e-114
			099727	TIM4_HUMAN Metalloproteinase inhibitor 4 precursor (TIMP-4) (Tissue inhibitor of metalloproteinases-4)	409	e-114
i I			AAB40391.1	tissue inhibitor of metalloproteinase 4	409	e-114
			AAC34422.1	tissue inhibitor of metalloproteinase 4	409	e-114
			AAH10553.1	AAH10553 tissue inhibitor of metalloproteinase 4.	409	e-114
	i ·		NP 003246.1	tissue inhibitor of metalloproteinase 2 precursor	216	3e-56
1			,			

		:	D16035	TIM2_HUMAN Metalloproteinase inhibitor 2 precursor (TIMP-2) (Tissue inhibitor of		
				Inclaim protein ascs-2) (CSC-21IA)	216	3e-56
			A37128	metalloproteinase inhibitor 2 precursor	216	3e-56
	-		AAB19474.1	tissue inhibitor of metalloproteinase 2; TIMP-2	216	L
	. [-	AAA59581.1	metalloproteinase inhibitor precursor	. 216	
	;		AAA61186.1	metalloproteinase-2 inhibitor precursor	216	
		•	AAC50729.1	tissue inhibitor of metalloproteinases-2	. 216	
			1GXD	C Chain C, Prommp-2TIMP-2 Complex	214	
·;			1GXD	D Chain D, Prommp-2TIMP-2 Complex	214	
			1BR9	Human Tissue Inhibitor Of Metalloproteinase-2	214	1e-55
			AAB24785.1	TIMP-2, CSC-21K=tissue inhibitor of metalloproteinase	211	9e-55
			AAA21815.1	metalloproteinase-3 tissue inhibitor	200	3e-51
			NP_000353.1	tissue inhibitor of metalloproteinase 3; Tissue inhibitor of metalloproteinase-3; K222 expressed in degenerative retinas	199	4e-51
. :		·	P35625	TIM3_HUMAN Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein)	199	4e-51
:	:	·	S45317	metalloproteinase inhibitor 3 precursor	199	
			AAA17672.1	tissue inhibitor of metalloproteinase-3 precurso	199	
,	. : .		CAA53813.1	tissue inhibitor of metalloproteinases-3	199	
	· .		AAB60373.1	tissue inhibitor of metalloproteinases-3	199	
			AAB34532.1	TIMP-3	199	
·			AAC50393.1	tissue inhibitor of metalloproteinases-3	199	L
	1		AAB07547.1	tissue inhibitor of metalloproteinase-3	199	
			AAH14277.1	AAH14277 Similar to tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory)	. 199	4e-51
			CAA38400.1	Tissue inhibitor of metalloproteinases, Type-2	199	
NM_008302 NP_032328.1	Mm.2180	U.(IR-D) 2.71	NP 031381.2	heat shock 90kDa protein 1, beta; heat shock 90kD protein 1, beta; Heat-shock 90kD protein-1, beta	1202	:

					-	
			P08238	HS9B HUMAN Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	1202	0
		1	AAA36026.1	90 kD heat shock protein	1202	
	ī		AAH04928.1	AAH04928 Unknown (protein for MGC:10493)	1007	
			AAH12807.1	AAH12807 Unknown (profein for MGC:3483)	1202	٥
λ,			AAH14485.1	AAH14485 Unknown (protein for MGC:23206)	1202	
			AAH16753.1	AAH16753 Unknown (protein for MGC:1138)	1202	
:		\	HHHU84	heat shock protein 90-beta [validated]	1197	C
		·	AAA36025.1	90kDa heat shock protein	1197	0
			1307197A	heat shock protein 90k	1197	0
			T46243	hypothetical protein DKFZp761K0511.1	1170	C
	: . ::,		CAB66478.1	hypothetical protein	1170	0
			NP 005339.1	heat shock 90kDa protein 1, alpha; heat shock 90kD protein 1, alpha	1099	0
			ннни86	heat shock protein 90-alpha	1099	0
			AAA63194.1	heat shock protein	1099	0
		() () ()	AAF82792,1	AF275719_1 chaperone protein HSP90 beta	1052	0
	·		AAH09206.1	AAH09206 heat shock 90kD protein 1, beta	1052	0
			AAH23006.1	Unknown (protein for MGC:30059)	961	0
.			AAH00987.1	AAH00987 Unknown (protein for IMAGE:3446372)	008	C
			AAC25497.1	Hsp89-alpha-delta-N	750	0
			AAH07989.1	AAH07989 Similar to heat shock 90kD protein 1, alpha	969	C
NM_009056 NP_033082.1 Mm.102	Mm.102	U:(R-D) 2.63	NP_602309.1	regulatory factor X2, isoform b; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	1166	
			P48378	RFX2_HUMAN DNA-binding protein RFX2	1153	٥
			B55926	DNA binding protein RFX2	1153	C
			CAA53705.1	DNA binding protein RFX2	1153	0
	,		NP_000626.2	regulatory factor X2, isoform a; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	1152	C

	.	,				
	. :	·	AAH28579.1	128579.1 regulatory factor X, 2 (influences HLA class II expression)	1151	C
_			NP_602304.1	regulatory factor X3 isoform b; DNA binding protein RFX3	777	
		,	AAH22191.1	AAH22191 Unknown (protein for MGC:3664)	773	0
	٠.,		NP 002910.1	regulatory factor X3 isoform a; DNA binding protein RFX3	751	C
			P48380 ·	RFX3_HUMAN DNA-binding protein RFX3	751	Î
		·	D55926	DNA binding protein RFX3	751	0
	· ,		CAA53706.1	DNA binding protein RFX3	751	C
	<i>L</i> .		P22670	RFX1_HUMAN MHC class II regulatory factor RFX1 (RFX) (Enhancer factor C) (EF-C)	989	C
			A35913	regulatory factor X	989	0
,	1		CAA41730.1	MHC class II regulatory factor RFX	989	0
			NP 002909.2	regulatory factor XI; trans-acting regulatory factor 1; enhancer factor C; MHC class II regulatory factor RFX	989	
			CAC88163.1	bA32F11.1.2 (regulatory factor X, 3 (influences HLA class II expression), putative isoform 2)	507	e-143
,		, (See and)	CAC88164.1	bA32F11.1.1 (regulatory factor X, 3 (influences HLA class Ilexpression), isoform 1)	486	e-136
NM_026346 NP_080622.1	Mm.4046 6	U:(IR-D) 2.28	NP_478136.1	F-box only protein 32 isoform 1; muscle atrophy F-box protein; atrogin-1	710	0
			Q969P5	FX32_HUMAN F-box only protein 32 (Muscle atrophy F-box protein) (MAFbx) (Atrogin-1)	710	0
			AAL16407.1	muscle atrophy F-box protein	710	0
			BAB71333.1	unnamed protein product	710	0
y - ; }		·	CAD12251.1	F-box only 32	710	0
			BAB85128.1	F-box domain Fbx25-containing protein	446	e-124
	100		NP 680482.1	F-box only protein 32 isoform 2; muscle atrophy F-box protein; atrogin-1	422	e-117
			AAH24030.1	similar to RIKEN cDNA 4833442G10 gene	417	e-116
			AAF04526.1	AF174605_1 F-box protein Fbx25	354	4e-97
			NP 036305:1	F-box only protein 25; F-box protein Fbx25	353	6e-97

		To state of				
NM_009244	T. F 102 41	(A)				
NP_033270.1	Mm.19341 U:(IK-D) 8 2.26	U:(IK-D) 2.26	AAA51547.1	alpha-1-antitrypsin precursor	508	e-144
			AAH15642.1	AAH15642 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	508	e-144
	٠ ٠		1012287A	antitrypsin alpha1 mutant	507	e-143
			P01009	A1AT_HUMAN Alpha-1-antitrypsin precursor (Alpha-1 protease inhibitor) (Alpha-1-antiproteinase) (PRO0684/PRO2209)	507	e-143
		·	ITHU	alpha-1-antitrypsin precursor [validated]	507	e-143
	,		CAA25838.1	alpha 1-antitrypsin	507	e-143
7			AAB59375.1	alpha-1-antitrypsin	· 507	e-143
	13		AAG35496.1	AF130117_27 PRO2209	507	e-143
A Y			NP_000286.2	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1; Protease inhibitor (alpha-1-antitrypsin); protease inhibitor 1 (anti-elastase), alpha-1-antitrypsin	909	e-143
:			AAH11991.1	AAH11991 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	206	e-143
			AAF29581.1	AF113676_1 PRO0684	504	e-142
			AAB59495.1	alpha-1-antitrypsin	504	e-142
,			ÄAA51546.1	alpha-1-antitrypsin	501	e-141
:			1HP7	Chain A, A 2.1 Angstrom Structure Of An Uncleaved Alpha-1- Antitypsin Shows Variability Of The Reactive Center And Other Loops	499	e-141
			1KCT	Alpha1-Antitrypsin	498	e-141
NM_009194 NP_033220.1	Mm.4168	U:(IR-D) 2.16	NP 001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters),	1978	0
			P55011	S122_HUMAN Solute carrier family 12 member 2 (Bumetanide-sensitive sodium-(potassium)-chloride cotransporter 1) (Basolateral Na-K-Cl symporter)	1978	0
ì	*;	; ²	A57187	burnetanide-sensitive Na-K-Cl cotransporter	1978	0
:			AAC 0561.1.	burnetanide-sensitive Na-K-Cl cottansporter	1978	0

\		,					
<u> </u>				AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1851	0
			*	NP 000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12 (sodium/potassium/chloride transporters),	1294	0
,				Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitiv sodium-(potassium)-chloride cotransporter 2) (Kidney-specific Na-K-Cl symporter)	1294	.0
* ;				AAB07364.1	bumetanide-sensitive Na-K-2CI cotransporter	1294	0
				NP_000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters)	1028	0
,			4	AAC50355.1	thiazide-sensitive Na-Cl	1028	0
				P55017	S123_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride cotransporter) (Na-Cl symporter)	1024	0
		,		G01202	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
				CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
		1		AAL32454.1	AF439152_1 sodium-potassium-chloride cotransporter	598	e-170
- :				PC4180	thiazide-sensitive sodium-chloride cotransporter	413	e-114
15 -				AAH40138.1	Similar to solute carrier family 12 (sodium/potassium/chloride	403	e-111
<u>. </u>				1008.1	cation-chloride cotransporter-interacting protein 1	261	
ZZ	NM_009254 NP_033280.1	Mm.2623	U:(IR-D) 2.15	04559.2	scrine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	549	:
		- 4	F	P35237	PTI6_HUMAN Placental thrombin inhibitor (Cytoplasmic antiproteinase) (CAP)(Protease inhibitor 6) (PI-6)	549	<u> </u>
ļ			-	AAB30320.1	cytoplasmic antiproteinase; CAP	549	e-156
				AAH01394.1	AAH01394 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6	549	e-156
<u>· · · · · · · · · · · · · · · · · · · </u>		,	<i>;</i>	A48681	placental thrombin inhibitor	548	e-156
لـــــ	-		·	CAA80373.1	thrombin inhibitor	548	e-156
				NP 002631.1	scrinc (or cysteinc) proteinase inhibitor, clade B (ovalbumin), member 8, protease inhibitor 8 (ovalbumin type)	459	e-129
	:	•					

, ,	.,		P50452	SPB8_HUMAN Cytoplasmic antiproteinase 2 (CAP2) (CAP-2) (Protease inhibitor 8)(Serpin B8)	450	9 100
	-		A59273	proteinase inhibitor 8	459	e-129
			AAC41939.1	cytoplasmic antiproteinase 2	459	e-129
			NP 004146.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)	445	P-175
		• •	P50453	SPB9_HUMAN Cytoplasmic antiproteinase 3 (CAP3) (CAP-3) (Protease inhibitor 9)(Serpin B9)	445	-175
;*			B59273	proteinase inhibitor 9	445	e-125
			AAC41940.1	cytoplasmic antiproteinase 3	445	e-125
			AAC50793.1	serine proteinase inhibitor	445	e-125
		·	AAH02538.1	AAH02538 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9	445	e-125
		:	BAB91078.1	serine protease inhibitor 9	445	e-125
)-' :			NP_109591.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	330	36.90
÷.			P30740	ILEU_HUMAN Leukocyte elastase inhibitor (LEI) (Monocyte/neutrophil elastase inhibitor) (MNREI) (EI)	330	3 6
			S27383	elastase inhibitor	330	36.00
			AAC31394.1	monocyte/neutrophil elastase inhibitor	330	36.90
		,	AAH09015.1	AAH09015 serine (or cysteine) proteinase inhibitor, clade B (ovalburnin), member 1	330	36-90
	· ' .		XP 036951.4	similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
			P48594	SCC2 HUMAN Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
				leupin	327	2e-89
			AAA97553.1	squamous cell carcinoma antigen 2	327	2e-89
			AAA92602.1	squamous cell carcinoma antigen	327	2e-89
			BAB21525.1	squamous cell carcinoma antigen 2	327	2e-89
			AAH17401.1	AAH17401 Unknown (protein for MGC:27150)	327	2e-89
			I38202	leupin precursor	327	2e-89
					, ,	20.02

	1					
	:		138201	squamous cell carcinoma antigen 1	325	. 7e-89
	\$1.5 \$1.5 \$1.5 \$1.5 \$1.5 \$1.5 \$1.5 \$1.5		NP 008850.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3; squamous cell carcinoma antigen 1	325	98-80
			P29508	SCC1_HUMAN Squamous cell carcinoma antigen 1 (SCCA-1) (Protein T4-A)	325	9e-89
		. Er	AAA86317.1	squamous cell carcinoma antigen	325	96-89
			AAA97552.1	squamous cell carcinoma antigen 1	325	9e-89
			AAH05224.1	AAH05224 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3	325	9e-89
	<i>:</i>	,	AAB20405.1	squamous cell carcinoma antigen; SCC antigen	325	96-89
NM_019431 NP_062304.1	Mm.1037 24	U:(IR-D) 2.09	NP_055220.1	voltage-dependent calcium channel gamma-4 subunit, neuronal voltage-gated calcium channel gamma-4 subunit	54 <u>0</u>	e-153
\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.			Q9UBN1	CCG4_HUMAN Voltage-dependent calcium channel gamma-4 subunit (Neuronal voltage-gated calcium channel gamma-4 subunit)	540	e-153
			AAF03090.1	calcium channel gamma 4 subunit	540	e-153
	 t	-	AAF14538.1	AF162692_1 putative voltage-gated calcium channel gamma-4 subunit	540	e-153
			AAH34532.1	calcium channel, voltage-dependent, gamma subunit 4	540	e-153
		·	NP_006069.1	voltage-dependent calcium channel gamma-2 subunit; stargazin; neuronal voltage-gated calcium channel gamma-2 subunit	303	2e-82
			869X6O	CCG2_HUMAN Voltage-dependent calcium channel gamma-2 subunit (Neuronal voltage-gated calcium channel gamma-2 subunit)	303	2e-82
			AAD22738.1	AF096322_1 neuronal voltage-gated calcium channel gamna-2 subunit	303	76-87
			AAL50049.1	AF361354_1 voltage-dependent calcium channel gamma-8 subunit	302	4e-82
	. :		NP_114101.4	voltage-dependent calcium channel gamma-8 subunit, neuronal voltage-gated calcium channel gamma-8 subunit	300	2e-81
			Q8WXS5	CCG8_HUMAN Voltage-dependent calcium channel gamna-8 subunit (Neuronal voltage-gated calcium channel gamma-8 subunit)	300	2e-81
			AAK20031.1	AF288388_1 calcium channel gamma subunit 8	300	2e-81
1	* ***		NP_006530.1	voltage-dependent calcium channel gamma-3 subunit; neuronal voltage-gated calcium channel gamma-3 subunit	298	8e-81
· \ \ .	: , ;		060359	CCG3_HUMAN Voltage-dependent calcium channel gamma-3 subunit (Neuronal voltage-gated calcium channel gamma-3 subunit)	298	8e-81

			A A C3504C 1	1 1		
			AAC12246.1	Unknown gene product	298	8e-81
			AAD22739.1	AF100346_1 neuronal voltage gated calcium channel gamma-3 subunit	298	8e-81
		·	AAF42975.1	AF134640_1 calcium channel gamma subunit 3	298	8e-81
	,		AAH40005.1	calcium channel, voltage-dependent, gamma subunit 3	298	8e-81
- 1	,	,	XP 050231.1	similar to calcium channel gamma subunit 8	270	2e-77
			AAK15019.1	AF234892_1 putative voltage gated calcium channel gamma-8 subunit CACNG8	2	
NM_019999 NP_064383.1	Mm.1772 72	U:(IR-D) 2.05	NP_072094.1	KIAA1184 protein	629	0
			AAH02937.1	AAH02937 Similar to hypothetical protein MNCh-5687	650	۶
			BAA86498.1	KIAA1184 protein	570	P-165
		3 ·	AAH36457.1	Unknown (protein for MGC:33461)	579	e-165
	1					
		1				
AK002297						1
	Mm.18130 U:(C-IR)	U:(C-IR)				-
BAB21996.1	2	6.3	NP 060464.1	060464.1 hypothetical protein FLJ10099		·
	·		BAA91444.1	unnamed protein product	620	e-177
	15.		AAH08675.1	hypothetical protein FL110099	620	e-177
			AAH12562.1	Similar to hypothetical protein FLJ10099	620	e-177
			AAH10519.1	Similar to hypothetical protein FLJ10099	385	e-106
	:	U:(C-IR) 6.11	NP_478137.1	zinc finger protein 354B	1031	0
NM 013744	Vm.7467	U.(IR-D)				
NP 038772.1	0	2.04			,	
		:	BAB71556.1	unnamed protein product	1031	0
	, , , , , , , , , , , , , , , , , , ,		AAD05335.1	zinc finger protein EZNF	958	C
			NP 005640.1	transcription factor 17	957	0
			060765	TC17_HUMAN Transcription factor 17 (Zinc finger protein eZNF)	957	C

			BAA95189 1	1 12/11		
	: '		NTD ANOMOR 1	rejun fin con annothing 104 (771111)	756	0
			-a :	ZINC LINGEL DOUGHL 104 (N. Iupper-like)	567	e-161
			AAH22992.1	Unknown (protein for MGC:29879)	567	e-161
	:		AAC51180.1	kruppel-related zinc finger protein	292	e-161
:			XP 166367.1	similar to Zinc finger protein 184	995	e-161
		-	929660	Z184_HUMAN Zinc finger protein 184	566	e-161
			CAA17278.1	b34I8.1 (zinc finger protein 184 (Kruppel-like))	566	e-161
			XP 032054.2		536	e-152
			AAK30252.1	AF352026_1 EZFIT-related protein 1	536	e-152
<i>:</i>	·		CAD38551.1	hypothetical protein	536	e-152
	·		XP_091988.1	similar to zinc finger protein 91 (HPF7, HTF10)	533	e-151
	-1 -		AAH36110.1	Similar to zinc finger protein 208	531	e-150
NM_018764 NP_061234.1	Mm.1196 4	U:(C-IR) 4.56	NP_002580.2	protocadherin 7, isoform a precursor; BH-pcdh; BH-protocadherin (brain-heart); brain-heart protocadherin	1856	0
1	·		060245	PCH7_HUMAN Protocadherin 7 precursor (Brain-heart protocadherin) (BH-Pcdh)	1855	0
			BAA25194.1	PCDH7 (BH-Pcdh)a	1855	0
	:		NP_115832.1	protocadherin 7, isoform b precursor; BH-pcdh; brain-heart protocadherin; BH-protocadherin (brain-heart)	1838	0
	1	:	T00041	BH-protocadherin PCDH7 (clone BH-Pcdh-b)	1837	0
			BAA25195.1	PCDH7 (BH-Pcdh)b	1837	0
·	1 1 1	-	NP_115833.1	protocadherin 7, isoform c precursor; BH-pcdh; brain-heart protocadherin; BH-protocadherin (brain-heart)	1691	0
			T00042	BH-protocadherin PCDH7 (clone BH-Pcdh-c)	1690	0
			BAA25196.1	PCDH7 (BH-Pcdh)c	1690	0
			NP_115796.1	protocadherin 1, isoform 2 precursor; protocadherin 42; cadherin-like protein 1	817	0
	1.		AAH35812.1	Similar to protocadherin 1 (cadherin-like 1)	816	0
	, i	3	NP 002578.1	protocadherin 1, isoform 1 precursor; protocadherin 42; cadherin-like protein 1	816	0
			Q08174	PCH1_HUMAN Protocadherin 1 precursor (Protocadherin 42) (PC42) (Cadherin-like protein 1)	816	0
,						

			ÄAA36419.1	protocadherin 42	816	0
			NP_065136.1	protocadherin 9 precursor; cadherin superfamily protein VR4-11	575	e-163
	* * * * * * * * * * * * * * * * * * * *	:	AAF89689.2	AF169692_I protocadherin-9	575	e-163
NM 008121	, . 1	U:(C-IR) 4.51				
	Mm.19038 U:(C-D) 1 6 2.06	U:(C-D) 2.06	NP_005257.2	gap junction protein, alpha 5, 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)	580	e-165
			P36382	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)	280	e-165
			AAA91833.1	connexin 40	280	e-165
			AAD37801.1	AF151979_1 connexin 40	280	e-165
			AAA60457.2	connexin40	580	e-165
			AAH13313.1	gap junction protein, alpha 5, 40kD (connexin 40)	580	e-165
		; ; ,	I38429	connexin40	575	e-164
			NP_068773.2	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)	301	16-81
:		,	CAC16957.1	bA26414.3 (novel connexin (gap junction protein)	301	16-81
			09У6Н8	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)	301	1e-81
	·	:	AAD42925.1	gap-junction protein alpha 3	301	1e-81
			NP_005258.1	gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)	299	4e-81
	:		139176	intrinsic membrane protein MP70	. 299	4e-81
		-	AAA77062.1	gap junction membrane channel protein alpha-8	299	4e-81
: , .			P48165	CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)	296	36-80
		·		AF217524_1 gap junction protein alpha 8	296	3e-80
			AAK55516.1	AF271261_1 connexin 58	282	5e-76
			NP_110399.1	connexin 59; gap junction alpha 10	282	5e-76
	2	·	P <i>57773</i>	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)	282	5e-76

			AAG09406.1	AF179597_1 connexin 59	282	5e-76
			AAD56533.1	AF180815_1 truncated connexin 37 polymorph	270	2e-72
		•	NP_115991.1	connexin 62	267	2e-71
			AAK51676.1	AF296766_1 connexin 62	267	2e-71
	•.		CAC93847.1	connexin62	267	2e-71
NTM 008314		U:(C-IR)				
+TC000 - TATAT		U:(C-D)				
NP_032340.1	Mm:4835	2.43	I37107	5-HT5A serotonin receptor	584	e-166
			CAA57168.1	5-HT5A serotonin receptor	584	e-166
	: .	3	AAM21132.1	AF498985_1 5-hydroxytryptamine receptor 5A	584	e-166
\			BAA94458.1	5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
			NP_000856.1	5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
	·		P28566	5H1E HUMAN 5-hydroxytryptamine 1E receptor (5-HT-1E) (Serotonin receptor) (5-HT1E) (S31)	212	2e-54
			A45260	serotonin receptor 1E	212	2e-54
			CAA77558.1	serotonin receptor	212	2e-54
	***		AAA58353.1	serotonin receptor	212	2e-54
		÷	AAA58355.1	serotonin receptor	212	2e-54
A.		•	CAC10582.1	bA76H14.2 (5-hydroxytryptamine (serotonin) receptor 1E)	212	2e-54
			AAM21127.1	AF498980_1 5-hydroxytryptamine receptor 1E	212	2e-54
,			NP_000857.1	5-hydroxytryptamine (serotonin) receptor 1F; 5-hydroxytryptamine receptor 1F	209	1e-53
	:		P30939	SH1F_HUMAN 5-hydroxytryptamine 1F receptor (5-HT-1F) (Serotonin receptor)	209	1e-53
			A47321	serotonin receptor 1F	209	1e-53
		į	AAA36605.1	serotonin receptor	209	1e-53
7.			AAA36646.1	serotonin receptor	209	1e-53
			AAM21128.1	AF498981_1 5-hydroxytryptamine receptor 1F	209	1e-53
	* 1		BAA90453.1	5-hydroxytryptamine (serotonin) receptor 1F	209	1e-53

			XP_003692.2	similar to 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotomin receptor) (5-HT1A) (G-21)	. 205	1e-52
		•	P08908	5H1A_HUMAN 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotonin receptor) (5-HT1A) (G-21)	205	1e-52
			I38209	serotonin receptor 1A	205	1e-52
			CAA40962.1	serotonin 5-HT1a receptor	205	1e-52
	- :		AAA66493.1	serotonin receptor	205	1e-52
. "	:		BAA94488.1	serotonin receptor 1A	205	1e-52
			AAM21125.1	AF498978 1 5-hydroxytryptamine receptor 1A	205	1e-52
			XP_092299.1	similar to KIAA0622 protein - human (fragment)	205	1e-52
			NP_000854.1	5-hydroxytryptamine (serotonin) receptor 1B; 5-HT1B; 5-HT1DB	204	2e-52
			P28222	5H1B_HUMAN 5-hydroxytryptamine 1B receptor (5-HT-1B) (Serotonin receptor)(5-HT-1D-beta) (Serotonin 1D beta receptor) (S12)	204	2e-52
			JN0268	serotonin receptor 1B	204	2e-52
		•	AAA58675.1	serotonin 1Db receptor	204	2e-52
	; ;		AAA36029.1	serotonin receptor	204	2e-52
			AAA36030.1	5-hyroxytryptamine 1D receptor	204	. 2e-52
			BAA01763.1	serotonin 1B receptor	204	2e-52
	. ,		AAA60316.1	serotonin 1D receptor	204	2e-52
		. ,	CAB51537.1	dJ501M23.1 (5-hydroxytryptamine (serotonin) receptor 1B)	204	2e-52
			BAA94455.1	5-hydroxytryptamine (serotonin) receptor 1B	204	2e-52
			2209242B	serotonin receptor:ISOTYPE=1D-beta	204	Że-52
	1		NP_000515.1	5-hydroxytryptamine (serotonin) receptor 1A	202	2e-51
		. i	CAA31908.1	receptor protein (AA 1 - 421)	202	2e-51
			AAA36440.1	guanine nucleotide-binding regulatory protein-coupled recepto	202	. 2e-51
			1311340A	G protein coupled receptor	202	2e-51

						•
NM 009183		U.(C-IR) 4.19	, , , , , , , , , , , , , , , , , , ,			,
NP_033209.1	Mm.10701	U:(C-D) 2.35	NP_005659.1	sialyltransferase 8D (alpha-2, 8-polysialytransferase); Polysialyltransferase; sialyltransferase 8 (alpha-2, 8-polysialytransferase) D	714	0
	} ; . !	<u>۴</u> .	092187	SIBD_HUMAN CMP-N-acetylneuraminate-poly-alpha-2,8-sialyl transferase (Alpha-2,8-sialyltransferase 8D) (ST8Sia IV) (Polysialyltransferase-1)	714	0
-	ı		I59403	alpha-2,8-polysialyltransferase	714	0
1			AAC41775.1	alpha-2,8-polysialyltransferase	714	0
	,		2116443A	polysialyltransferase	714	0
			NP_006002.1	sialyltransferase 8B (alpha-2, 8-sialytransferase); Sialyltransferase X; sialyltransferase 8 (alpha-2, 8-sialytransferase) B	429	e-119
		,	Q92186	SI8B_HUMAN Alpha-2,8-sialyltransferase 8B (ST8Sia II) (Sialyltransferase X)(STX)	429	e-119
		,	I39169	sialyltransferase	429	e-119
:			AAC24458.1	sialyltransferase	429	e-1:19
· .	·	•	AAB51242.1	sialyltransferase X	429	e-119
			2123358A	sialyltransferase STX	429	e-119
	:		B54898	STX protein	330	2e-89
			AAA36613.1	sialyltransferase	330	2e-89
-		÷	AAH27866.1	Similar to sialyltransferase 8D (alpha-2, 8-polysialytransferase)	320	1e-86
		:	AAC15901.1	alpha-2,8-sialyltransferase III	219	3e-56
	1		NP_056963.1	sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase); alpha-2,8-sialyltransferase III	215	. 8e-55
· ;			043173	SISC_HUMAN Sia-alpha-2,3-Gal-beta-1,4-GlcNAc-R:alpha 2,8-sialyltransferase (Alpha-2,8-sialyltransferase 8C) (ST8Sia III)	215	8e-55
	Co.	· ·	AAB87642.1	Sia alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase	215	8e-55
NM_009520	1	U:(C-IR) 4.15 U:(C-D)		wingless-type MMTV integration site family, member 2B, isoform WNT-2B2, wingless-type MMTV integration site family member 13. XWNT2. Xenome	-	
NP_033546.1 Mm.10740 3.21	Mm.10740		NP_078613.1	homolog of	726	0
			093097	WN2B HUMAN WNT-2B protein precursor (WNT-13)	726	0

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	# .		BAB11985.1	311985.1 WNT-2B Isoform 2	726	0
			NP_004176.2	wingless-type MMTV integration site family, member 2B, isoform WNT-2B1; wingless-type MMTV integration site family, member 13; XWNT2, Xenopus, homolog of	702	0
			BAB11984.1	WNT-2B Isoform 1	702	0
			T09612	secreted glycoprotein Wnt-13	969	0
	1		CAA96283.1	Wnt-13	969	0
			NP 003382.1	wingless-type MMTV integration site family member 2 precursor; int-1 related protein; oncogene INT1-like 1; secreted growth factor	535	9.152
			P09544	WNT2_HUMAN WNT-2 protein precursor (RR protein) (Int-1 related protein)	535	e-152
1 to 1			S00834	int-1-like protein 1 precursor	535	e-152
			CAA30725.1	Irp protein (AA 1-360)	535	e-152
		,	AAH29854.1	wingless-type MMTV integration site family member 2	535	e-152
			AAB67043.1	secreted growth factor	404	e-112
			NP_003383.1	wingless-type MMTV integration site family, member 5A precursor; proto-oncogene Wnt-5A precursor; WNT-5A protein precursor	360	2e-99
			P41221	WN5A_HUMAN WNT-5A protein precursor	360	2e-99
	::		A48914	proto-oncogene Wnt-5A precursor	360	2e-99
			AAA16842.1	hWNT5A	360	2e-99
			NP_116031.1	wingless-type MMTV integration site family, member 5B precursor; WNT-5B protein precursor	358	16-98
			NP_110402.2	wingless-type MMTV integration site family, member 5B precursor;	: 358	1e-98
3 1 · 1			WNT-5B			
			precursor	1	358	1e-98
		,	Q9H1J7	WNSB_HUMAN WNT-5B protein precursor	358	1e-98
			AAH01749.1	AAH01749 Similar to wingless-related MMTV integration site 5B	358	16-98
			BAB62039.1	WNT5B	358	16-98
,			NP 478679.1	wingless-type MMTV integration site family, member 7B precursor	355	1e-97

			P56706	WN7B_HUMAN WNT-7B protein precursor	355	1e-97
* 1	; ;		BAB68399.1	WNT7B	355	1e-97
		1	AAH34923.1	wingless-type MMTV integration site family, member 7B	355	1e-97
			AAN32640.1	AF416743_1 WNT7B	355	1e-97
}.			NP_004616.2	wingless-type MMTV integration site family, member 7A precursor; proto-oncogene Wnt/a protein.	348	16.05
	-		AAH08811.1	Unknown (protein for MGC:10346)	348	1e-95
			AAG38659.1	WNT5b precursor	348	20-05
· · · · · · · · · · · · · · · · · · ·	:	U:(C-IR)				3
		3.61 U:(C-D)				•
AK011231		2.66				: :
BAB27481.1	Mm.22533	U:(IR-D) 2.42	NP_055330.1	CCR4-NOT transcription complex, subunit 2; NOT2 (negative regulator of transcription 2, yeast) homolog	877	C
			AAF29827.1	AF180473_1 Not2p	877	2 0
7		-	AAH02597.1	CCR4-NOT transcription complex, subunit 2	877	0
	1		AAH11826.1	Similar to CCR4-NOT transcription complex, subunit 2	877	0
			BAA91313.1	unnamed protein product	751	0
			AAF29095.1	AF161480_1 HSPC131	729	0
			AAG39297.1	AF113226_1 MSTP046	728	0
		. "	T46494	hypothetical protein DKFZp434M0572.1	326	86-89
			CAB70869.1	hypothetical protein	326	8e-89
2,000		U:(C-IR)				
NP_033743.1	5.6 U:(C-D) Mm.89854 2.86	3.6 U:(C-D) 2.86	NP 002381.2	a disintegrin and metalloprotease domain 11, isoform 1 preproprotein; metalloproteinase-like, disintegrin-like, costeine-rich motein	1454	, c
	11: 11:		BAA32352.1	MDC/ADAM11	1454	0
			075078	AD11_HUMAN ADAM 11 precursor (A disintegrin and metalloproteinase domain 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein) (MDC)	1451	0
	:		165967	disintegrin-like metalloproteinase (BC 3.4.24), splice form 2	1345	0

						•
	:		BAA06670.1	metalloprotease/disintegrin-like protein	1340	C
			NP_067625.1	a disintegrin and metalloprotease domain 11, isoform 2 preproprotein; metalloproteinase-like, disintegrin-like, cysteine-rich protein	1011	
		,	S38539	disintegrin-like metalloproteinase (EC 3.4.24), splice form 1	1011	0
			AAB29191.1	MDC=metalloprotease/disintegrin-like cysteine-rich protein [human, cerebellum, Peptide, 524 aa]	1011	C
		4	BAA04213.1	MDC protein	1011	0
			BAA06671.1	metalloprotease/disintegrin-like protein	1008	0
		•	NP_068367.1	a disintegrin and metalloproteinase domain 22 isoform 5 proprotein; MDC2 delta	825	0
	:		BAA32350.1	MDC2 beta	825	0
			AAF22476.2	AF073291_1 MDC2	825	0
	. 1		NP_057435.2	a disintegrin and metalloproteinase domain 22 isoform 3 proprotein; MDC2 delta	825	0
			NP_068368.2	a disintegrin and metalloproteinase domain 22 isoform 2 proprotein; MDC2 delta	825	0
AK002979		U:(C-IR) 3.58				
BAB22492.1	Mm.19588 U.(C-D)	U:(C-D)	NP 056537 1	no lovon	(1
				DIP HUMAN D1 doparnine recentor-interacting protein calcum	330	26-92
,			AAF34714.1	AF225903 1 D1 doparnine receptor interacting protein calcyon	336	5P-02
			AAH38978.1	Similar to calcyon; D1 doparnine receptor-interacting protein	336	5e-92
NM 008714		U:(C-IR) 3.55			5	
NP_032740.1	Mm.31255		P46531	NTC1_HUMAN Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hN1) (Translocation-associated notch protein TAN-1)	4646	C
	1		AAG33848.1	AF308602_1 NOTCH 1	4646	0
			A40043	notch protein homolog TAN-1 precursor	4528	0
			AAA60614.1	TAN1	4482	0
3				notch 2 preproprotein	2628	0
			AAG37073.1	AF315356_1 NOTCH2 protein	2627	0

	1					
				NTC2_HUMAN Neurogenic locus notch homolog protein 2 precursor (Notch 2)		
			Q04721	(hN2)	2627	0
			AAA36377.2	NOTCH 2	2627	0
			AAC14346.1	Notch3	2065	0
			NP_000426.1	Notch homolog 3	2065	0
		X	Q9UM47	NTC3_HUMAN Neurogenic locus notch homolog protein 3 precursor (Notch 3)	2065	0
			S78549	notch3 protein	2065	0
		,	AAB91371.1	Notch3	2065	0
		,	AAC15789.1	Notch 3	2065	0
			NP_004548.1	Notch homolog 4 (Drosophila); Notch, drosophila, homolog of, 4; Notch (Drosophila) homolog 4	1023	0
			099466	NTC4_HUMAN Neurogenic locus notch homolog protein 4 precursor (Notch 4) (hNotch 4)	1023	0
		. `\	AAC32288.1	Notch4	1023	0
AK012553		U:(C-IR) 3.54				
BAB28313.1	U:(C-D Mm.45628 2.46	U.(C-D) 2.46	NP_001575.1	chromosome 11 open reading frame 8; 239FB	627	e-180
		# 1	Q1 <i>5777</i>	239F_HUMAN Fetal brain protein 239	627	e-180
,			AAC50564.1	239FB gene product	627	e-180
		*,5=	AAH31582.1	chromosome 11 open reading frame 8	. 627	e-180
			2122285A	239FB gene	627	e-180
	,		NP_001576.2	chromosome 22 open reading frame 1; 239AB	518	e-147
			015442	239A_HUMAN Adult brain protein 239	518	e-147
			AAC51673.2	239AB	518	e-147
	4		8035.1	Unknown (protein for MGC:40027)	518	e-147
			CAC48257.1	dJ873F21.1 (brain protein 239)	284	2e-76
		· v.	CAC10467.1	dJ710M3.1 (chromosome 11 open reading frame 8(Fetal brain protein 239))	253	5e-67

	3 e-160		3 e-160		3 e-160	7 5e-50	7 5e-50	7 5e-50	7 5e-50	5 6e-50		0	0	0	0	0	0	0	0	0	0	0	
	563	563	563	563	563	197	197	197	197	196		1192	1192	1191	1191	1165	. 728	728	728	728	728	714	
of the second of	amenomentum receptor, C-protem-coupled receptor similar to the agrenomedulin. 1 receptor.	ADMR_HUMAN Adrenomedullin receptor (AM-R)	adrenomedullin receptor	1 G-protein coupled receptor	1 adrenomedullin receptor	RDC1_HUMAN G protein-coupled receptor RDC1 homolog	G protein-coupled receptor RDC1	1 orphan receptor	2 similar to G protein-coupled receptor RDC1 homolog	1 Unknown (protein for MGC:33224)		ARN2_HUMAN Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2)			1 KIAA0307	1 Unknown (protein for MGC:33872)	1 aryl hydrocarbon receptor nuclear translocator	ARNT_HUMAN Aryl hydrocarbon receptor nuclear translocator (ARNT protein) (Dioxin receptor, nuclear translocator) (Hypoxia-inducible factor 1 beta) (HIF-1 beta)	aryl hydrocarbon receptor nuclear translocator Arnt [imported]	1 Arnt	aryl hydrocarbon receptor nuclear translocator, ARNT	1 hypothetical protein	
·	NP_009195.1	015218	JC5784	CAA73910.1	AAH34761.1	P25106 -	A39714	AAA62370.1	XP_051522.2	AAH36661.1	,	Q9HBZ2	AAG15310.1	NP_055677.1	BAA20766.1	AAH36099.1	NP_001659.1	P27540	159550	AAA51777.1	CAC21446.1	CAD38953.1	
U:(C-IR) 3.52 II:(C D)	3.08		•					1	,		II·(C-IR)	3.41		1-							i i	•	
	Mm.2857	,								,	Ξ,	Mm.4813	,	,						*		:	
NM_007412	NP_031438.1		·					,		: :	NM_007488	NP_031514.1	-										

2e-81	2e-81	2e-81	2e-81	2e-81	3e-81	5e-81	5e-81	Γ		- 6	0	0	0	0	96-91	96-91	9e-91	1e-88	4e-51	4e-51	51	15	51
	2e-	.2e	2e-	2e	3e	Şe.	Şe	,							96	96	96		4e-	4e-	4e-51	4e-51	4e-51
301	301	301	301	301	301	300	300	111		1345	1345	1345	1345	1345	333	333	333	326	201	201	201	. 201	201
BMAL. HUMAN BMAL1 protein (Brain and muscle ARNT-like 1) (Member of PAS protein 3) (Basic-helix-loop-helix-PAS orphan MOP3) (BHLH-PAS protein JAP3)	BMAL1a	2 aryl hydrocarbon receptor nuclear translocator-like	bHLH-PAS protein JAP3	basic-helix-loop-helix-PAS orphan MOP3	PAS protein 3	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1b	BMAL1b			1 RAB6 interacting, kinesin-like (rabkinesin6)	RB6K_HUMAN Rabkinesin-6 (RAB6-interacting kinesin-like protein) (GG10_2)	:	AF153329_1 RAB6KIFL	AAH12999 Similar to RAB6 interacting, kinesin-like (rabkinesin 6)	1 M-phase phosphoprotein 1; mitotic kinesin-like protein	hypothetical protein DKFZp434B0435.1	hypothetical protein	mitotic kinesin-related protein	kinesin-like 5 isoform 2; mitotic kinesin-like 1	KNS5_HUMAN Mitotic kinesin-like protein-1 (Kinesin-like protein 5)	• •	1 kinesin-like 5 isoform 1; mitotic kinesin-like 1	AAH17705 kinesin-like 5 (mitotic kinesin-like protein 1)
000327	BAA19968.1	NP_001169.2	AAB37248.1	AAC24353.1	AAC51213.1	JC5405	BAA19935.1	· ·		NP_005724.1	095235	AAC83230.1	AAD37806.1	AAH12999.1	NP_057279.1	T17272	CAB55962.1	BAB69456.1	NP 004847.2	Q02241	CAA47628.2	NP_612565.1	AAH17705.1
	•	. :		•				U:(C-IR)	3.26	U:(C-D) 2.41			. :				.				,	·	
		Î		`\ \ .\				U:(C-R)		Mm.19663 8							,				*		•
					1				NM_009004	NP_033030.1		N. 41 10 10 10 10 10 10 10 10 10 10 10 10 10					\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	1	1			12	

			ī			
NM 007730		U:(C-IR) 3.18				
		U:(C-D)			,	
NF_031/56.1	Mm.3819	2.18		NP_004361.2 alpha 1 type XII collagen, long isoform precursor	5003	0
			099715	CA1C_HUMAN Collagen alpha 1(XII) chain precursor	4987	0
-			AAC51244.1	collagen type XII alpha-1	4987	0
			NP_542376.1	alpha 1 type XII collagen, short isoform precursor	2961	0
			CAB71222.1	df238D15.1 (collagen, type XII, alpha 1)	2769	0
			CAB65984.1	dJ234P15.1 (collagen, type XII, alpha 1)	1046	0
		` 	AAC01506.1	type XII collagen	. 893	0
			A40970	undulin 1	518	e-146
			AAA36794.1	undulin 1	518	e-146
. V.		1	CAA72402:1	collagen type XIV	497	e-139
	1		CAC19497.1	bA209D8.1 (collagen type XII, alpha 1)	464	e-129
, ,			AAH14640.1	Unknown (protein for MGC:15451)	461	e-129
		U.(C-IR)	A35175	mucin 1 precursor, repetitive splice form A [validated]	370	e-102
NM_013605 NP_038633.1	Mm.1619 3	3.1/ U:(C-D) 3.4			**	
्र क्षे			NP_002447.2	mucin 1, transmembrane; peanut-reactive urinary mucin; episialin; polymorphic epithelial mucin; epithelial membrane antigen; DF3 antigen; TA23 antigen	368	e-101
• :	1"; :::		P15941	MUC1_HUMAN Mucin 1 precursor (MUC-1) (Polymorphic epithelial mucin) (PEM)	368	e-101
				(Turnor-associated epithelial membrane antigen) (EMA) (H23AG) (Peanut-reactive uninary mucin) (PIM) (Peant-cactive uninary mucin) (PIM) (Peant comments)		
			AAA60019.1	mineral factors (2017) (2017) (2017) (2017) (2017) (2017) (2017) (2017) mulcin	368	e-101
			CAA36478.1	precursor polypeptide (AA -21 to 494)	325	2e-88
7			AAA59876.1	polymorphic epithelial mucin	317	4e-86
			AAB53150.1	polymorphic epithelial mucin	317	4e-86
	·	***	XP 053256.8	similar to polymorphic epithelial mucin	317	4e-86
	•					

			AAA35805.1	episialin variant A precursor	298	2e-80
			AAA35807.1	episialin variant B precursor	298	2e-80
			AAD10858.1	MUC-1/Z mucin short variant	274	5e-73
			S48146	mucin 1 precursor, non-repetitive splice form Y [validated]	272	1e-72
1	ŕ		CAA56734.1	MUCI	272	1e-72
	ı.		AAD10857.1	010857.1 MUC-1/Y mucin short variant	272	1e-72
1			AAD27842.1	AF125525_1 MUC1/Y mucin precursor	271	3e-72
			AAD10856.1	AAD10856.1 MUC-1/X mucin short variant	214	4e-56
NM_008652		U:(C-IR) 3.11				
NP_032678.1	Mm.4594	U:(C-D) 2	NP_002457.1	v-myb myeloblastosis viral oncogene homolog (avian)-like 2; B-MYB; v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	0
-		,	P10244	MYBB_HUMAN Myb-related protein B (B-Myb)	1123	0
	٠.		S01991	transforming protein B-myb	1123	0
-			CAA31655.1	B-myb protein (AA 1-700)	1123	0
			CAC08392.1	dJ1028D15.3 (v-myb avian myeloblastosis viral oncogene homolog-like 2)	1123	0
1.31	,		AAH07585.1	v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	0
			P10243	MYBA_HUMAN Myb-related protein A (A-Myb)	280	1e-74
		:	S03423	transforming protein A-myb	. 280	1e-74
			CAA31656.1	A-myb N-terminal region)2341 is 2nd base in codon)	280	1e-74
	\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \		AAB49038.1	alternatively spliced product using exon 9A	276	1e-73
			CAA36371.1	MYB protein (AA 1-637)	276	1e-73
į		,		v-myb myeloblastosis viral oncogene homolog (avian); v-myb avian myeloblastosis viral oncogene homolog; Avian myeloblastosis viral (v-myb) oncogene homolog;		
, .			NP 005366.1	c-myb	276	1e-73
			AAA52032.1	c-myb	276	1e-73
			XP_004256.3	similar to Myb proto-oncogene protein (C-myb)	276	1e-73
			P10242	MYB_HUMAN Myb proto-oncogene protein (C-myb)	276	1e-73
The Table of the second		·\ :	AAB49039.1	c-myb gene product	276	1e-73
			•	.		

						-
	· .	1.	AAC96326.1	MYB proto-oncogene protein	276	1e-73
			TVHUMB	transforming protein myb, splice form containing exon 9A	276	1e-73
		Ì	AAB49035.1.	alternatively spliced product using exon 9B	276	1e-73
			AAB49036,1	alternatively spliced product using exon 8A	276	1e-73
	* .	U:(C-R)				
		2.99			•	
NTM 008168		U.(C-D)				·.
OOTOO TATA		U.(IR-D)		GLK5_HUMAN Glutamate receptor, ionotropic kainate 5 precursor (Glutamate		1 .
NP_032194.1	Mm.2879	2.41	Q16478	receptor KA-2) (KA2) (Excitatory amino acid receptor 2) (EAA2)	1757	0
; ;	3		157936	glutamate receptor subunit	1757	0
	7		AAB22591.1	glutamate receptor subunit, EAA2; excitatory amino acid receptor 2	1757	0
		:	NP_002079.2	glutamate receptor, ionotropic, kainate 5	1625	0
	:		CAC80547.1	kainate receptor subunit KA2a	1625	0
		!	NP_055434.1	glutamate receptor, ionotropic, kainate 4; excitatory amino acid receptor 1	1254	0
			Q16099	GLK4_HUMAN Glutamate receptor, ionotropic kainate 4 precursor (Glutamate receptor KA-1) (KA1) (Excitatory amino acid receptor 1)(EAA1)	1254	0
			JH0826	glutamate ionotropic receptor EAA1 chain precursor	1254	0
	-		AÄB29311.1	excitatory amino acid receptor 1; kainate receptor subunit EAA1	1254	0
			A54260	glutamate receptor 6 kainate-preferring precursor	704	0
1	•		AAB31362.1	GluR6 kainate receptor=ionotropic-type glutamate receptor	704	0
			NP_068775.1	glutamate receptor, ionotropic, kainate 2	704	0
			Q13002	GLK2_HUMAN Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4)	704	0
			AAC50420.1	EAA4	704	0
٠	,		CAC67487.1	GluR6 kainate receptor	689	Ö
			CAC81020.1	kainate receptor subunit	289	0
	1	·	Q13003	GLK3_HUMAN Glutamate receptor, ionotropic kainate 3 precursor (Glutamate receptor 7) (GluR-7) (GluR7) (Excitatory amino acid receptor 5) (EAA5)	289	0
			NP 000822.1	glutamate receptor, ionotropic, kainate 3	687	0

	:		AAB60407.1	BAA5	687	0
,	\$ 1 =	,	AAA95961.1	EAA3	685	0
U:(C-IR)	\\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\	U.(C-IR) 2.93				
NP_031791.1	Mm.22695	U.(C-D) 2.6	NP_001304.1	collapsin response mediator protein 1; collapsin response mediator protein 1 (dihydropyrimidinase-like 1)	.1036	
	1,		014194	DPY1_HUMAN Dihydropyrimidinase related protein-1 (DRP-1) (Collapsin response mediator protein 1) (CRMP-1)	1036	C
			JC5316	dihydropyrimidinase related protein 1	1036	0
			BAA11190.1	dihydropyrimidinase related protein-1	1036	0.
			AAH00252.1	collapsin response mediator protein 1	1036	0
		.1	AAH07613.1	collapsin response mediator protein 1	1036	0
			AAK55500.1	collapsin response mediator protein 1	696	0 .
			AAA93201.1	hCRMP-1	919	0
			NP_001377.1	dihydropyrimidinase-like 2; collapsin response mediator protein hCRMP-2	847	0
32.			Q16555	DPY2_HUMAN Dihydropyrimidinase related protein-2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3)	847	0 :
			JC5317	dihydropyrimidinase-related protein 2	847	0
			AAA93202.1	hCRMP-2	847	0
	A SAME AND A		BAA11191.1	dihydropyrimidinase related protein-2	847	0
		ويعيم	AAC05793.1	N2A3	847	0
			BAA86991.1	dihydropyrimidinase related protein 2	847	0
	*		NP_001378.1	dihydropyrimidinase-like 3	813	0
			Q14195	DPY3_HUMAN Dihydropyrimidinase related protein-3 (DRP-3) (Unc-33-like phosphoprotein) (ULIP protein) (Collapsin response mediator protein 4) (CRMP-4)	813	0
			JC5318	dihydropyrimidinase related protein 3	813	0
P			BAA11192.1	dihydropyrimidinase related protein-3	813	0
		:	AAH39006.1	dihydropyrimidinase-like 3	813	0
		· · · ·	CAA69153.1	ULP	810	0

		f	NP_006417.1	dihydropyrimidinase-like 4	. 781	0
-		1	014531	DPY4_HUMAN Dihydropyrimidinase related protein-4 (DRP-4) (ULIP4 protein)	781	0
:	:		BAA21886.1	dihydropyrimidinase related protein 4	781	0
`	·. ·	-	CAA71872.1	cytosolic phosphoprotein	749	0
		:	AAH07898.1	Similar to collapsin response mediator protein 1	712	0
NM 009872		U:(C-IR) 2.86				
_ NP_034002.1	Mm.15383 U:(C-D) 3 2.61	U:(C-D) 2.61	NP_003927.1	cyclin-dependent kinase 5, regulatory subunit 2; cyclin-dependent kinase 5 activator isoform p39i; NEURONAL CDK5 activator isoform	483	e-136
	1		013319	CD5S_HUMAN Cyclin-dependent kinase 5 activator 2 precursor (CDK5 activator 2) (Cyclin-dependent kinase 5 regulatory subunit 2) (P39)(P391)	483	P-136
400			139172	cyclin-dependent kinase 5 activator isoform p39i	483	e-136
		•	AAC50278.1	cyclin-dependent kinase 5 activator isoform p39i	483	e-136
	1		2202258A	cyclin-dependent kinase 5	483	e-136
			NP_003876.1	cyclin-dependent kinase 5, regulatory subunit 1; regulatory partner for cdk5 kinase; TPKII regulatory subunit	228	1e-59
· 1	(* 1		Q15078	CD5R_HUMAN Cyclin-dependent kinase 5 activator 1 precursor (CDK5 activator 1) (Cyclin-dependent kinase 5 regulatory subunit 1) (Tau protein kinase II 23 kDa subunit) (TPKII regulatory subunit) (P23) (P25) (P35)	. 228	1e-50
		:	S50861	cyclin-dependent kinase 5 regulatory chain p35	228	1e-59
	-		CAA56587.1	regulatory partner for cdk5 kinase	228	1e-59
1	,		AAH20580.1	AAH20580 cyclin-dependent kinase 5, regulatory subunit 1 (p35)	228	1e-59
			2019431A	cyclin-dependent kinase 5:SUBUNIT=p35	228	1e-59
	\.	:	AAH26347.1	cyclin-dependent kinase 5, rėgulatory subunit 1 (p35)	226	4e-59
			AAH30792.1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)	226	4e-59
			1H4L	D Chain D, Structure And Regulation Of The Cdk5-P25(Nck5a) Complex	217	2e-56
	i.		1H4L	E Chain E, Structure And Regulation Of The Cdk5-P25(Nck5a) Complex	217	2e-56

		U:(C-取)	XP_093388.1	similar to DnaJ homolog subfamily B member 8 (mDJ6)	336	4e-92
NM_019964 NP_064348.1	Mm.2039 U.(C-D) 2 3.13	2.84 U.(C-D) 3.13	· .			,
			NP_699161.1	hypothetical protein MGC33884	336	4e-92
			AAH29521.1	Similar to DnaJ (Hsp40) homolog, subfamily B, member 8	336	4e-92
			NP_005485.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform b; Heat shock protein J2	258	7e-69
		¥,	BAA32209.1	MRJ	258	7e-69
		·	AAD43194.1	AF075601_1 heat shock J2 protein	258	7e-69
			AAF21257.1	AF060703_1 DNAj homolog	258	7e-69
		1	BAA88770.1	DnaJ homolog	258	7e-69
			CAB66642.1	hypothetical protein	258	7e-69
			AAH00177.1	AAH00177 Similar to DnaJ (Hsp40) homolog, subfamily B, member 6	258	7e-69
	,	7	XP_052862.4	52862.4. similar to DnaJ homolog	256	3e-68
		* 1	NP 490647.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform a; Heat shock protein J2	249	99-99
			075190	DJB6_HUMAN DnaJ homolog subfamily B member 6 (Heat shock protein 12) (HSJ-2) (MSJ-1) (HHDJ1) (MRJ)	249	99-99
		!	BAA88769.1	DnaJ homolog	249	99-99
			AAH02446.1	AAH02446 MRJ gene for a member of the DNAJ protein family	249	99-99
NM 008417		U:(C-IR) 2.82				·
NP_032443.1	U:(C Mm.56930 2.47	U:(C-D) 2.47	NP_004965.1	potassium voltage-gated channel, shaker-related subfamily, member 2; voltage-gated potassium channel protein Kv1.2; potassium channel	880	. 0
			P16389	CIK2_HUMAN Potassium voltage-gated channel subfamily A member 2 (Potassium channel Kv1.2) (RBK2) (HBK5) (NGK1) (MK2) (HUKIV)	880	0
•			177466	potassium channel	880	0
			AAA36141.1	potassium channel	880	0
		,	NP_000208.1	potassium voltage-gated channel, shaker-related subfamily, member 1	662	0
	1		Q09470	CIK1_HUMAN Potassium voltage-gated channel subfamily A member 1 (Potassium channel Kv1.1) (HUKI) (HBK1)	662	0

-			157680	potassium channel KCNA1	662	0
	-		AAA36139,1	potassium channel	662	0
			NP_002223.2	potassium voltage-gated channel, shaker-related subfamily, member 3; potassium channel protein; voltage-gated potassium channel; voltage-gated potassium channel protein Kv1.3; type n potassium channel	009	e-171
1			P22001	CIK3_HUMAN Potassium voltage-gated channel subfamily A member 3 (Potassium channel Kv1.3) (HPCN3) (HGK5) (HUKIII) (HLK3)	009	e-171
			AAB88073.1	voltage-gated potassium channel	009	e-171
	j.		AAH35059.1	potassium voltage-gated channel, shaker-related subfamily, member 3	009	.e-171
-			A38101	potassium channel KCNA3	599	e-171
	1		AAA59457.1	potassium channel protein	. 599	e-171
	1:		AAC31761.1	potassium channel	598	e-171
			AAA36425.1	potassium channel protein	595	e-170
1.		Y		potassium voltage-gated channel, shaker-related subfamily, member 4; potassium voltage-gated channel, shaker-related subfamily, member 4-like; potassium channel KCNA4; shaker-related potassium channel Kv1.4; voltage-gated potassium channel;		
			NP_002224.1	potassium channel protein; type A potassium channel; rapidly inactivating potassium channel; fetal skeletal muscle potassium channel; cardiac potassium channel; potassium channel 2; voltage-gated potassium channel protein Kv1.4	543	e-154
			A39922	potassium channel KCNA4	543	e-154
:			AAA36140.1	potassium channel	543	e-154
			AAA61275.1	voltage-gated potassium channel	543	e-154
		1	P22459	CIK4_HUMAN Potassium voltage-gated channel subfamily A member 4 (Potassium channel Kv1.4) (HK1) (HPCN2) (HBK4) (HUKII)	. 541	e-153
		\	AAA60034.1	potassium channel protein	541	e-153
			NP_002226.1	potassium voltage-gated channel, shaker-related subfamily, member 6; voltage-gated potassium channel protein Kv1.6; human brain potassium channel-2	519	e-147
			P17658	CIK6_HUMAN Potassium voltage-gated channel subfamily A member 6 (Potassium channel Kv1.6) (HBK2)	519	e-147
			CAA35623.1	put. HBK2 protein (AA 1-529)	519	e-147
			S12787	potassium channel KCNA2	517	e-146

		U:(C-R)	NP_000757.2	000757.2 cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 13	563	e-160
NM_013809 NP_038837.1	Mm.7023 12	2./9 U:(C-D) 2.22			, ,	
			AAG35775.1	cytochrome P450 2A13	563	e-160
-			Q16696	CPAD_HUMAN Cytochrome P450 2A13 (CYPIIA13)	_558	e-158
			AAB40519.1	cytochrome P450	558	e-158
		·	O4HUA6	coumarin 7-hydroxylase (EC 1.14.14) cytochrome P450 2A6	555	e-158
			AAA52067.1	cytochrome P450IIA3	555	e-158
			NP_000753.2	cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 6; coumarin 7-hydroxylase; cytochrome P450, subfamily IIA (phenobarbital-inducible), nolynentide 3; xenobiotic monoxygenase: flavourotein linked monoxygenase.	553	e-157
			P11509	CPA6_HUMAN Cytochrome P450 2A6 (CYPIIA6) (Coumarin 7-hydroxylase) (IIA3) (CYP2A3) (P450(I))	552	e-157
:			CAA32118.1	P-450 IIA4 protein (AA 1-494)	552	e-157
-	, ,	•	AAF13600.1	AF182275_1 cytochrome P450-2A6	551	e-157
			1609083A	cytochrome P450IIA	551	e-156
		,	CAA32097.1	cytochrome P-450IIA (AA 1 - 489)	551	e-156
			P20853	CPA7_HUMAN Cytochrome P450 2A7 (CYPIIA7) (P450-IIA4)	543	e-154
			AAA52138.1	cytochronie P450IIA4	543	e-154
+	• ,		C34271	cytochrome P450 2A4	543	e-154
,		U:(C-IR) 2.74	NP_003890.1	Rho guanine nucleotide exchange factor 7 isoform a; SH3 domain-containing proline-rich protein: PAK-interacting exchange factor heta	1135	0
NM_017402 NP_059098.1	Î	U:(C-D) 2.8	: .			
	1		Q14155	PIXB_HUMAN Rho guanine nucleotide exchange factor 7 (PAK-interacting exchange factor beta) (Beta-Pix) (COOL-1) (p85)	1135	0
	,	100	BAA09763.1	The KIAA0142 gene is related to human KIAA0006 gene.	1135	0
			CAD38906.1	hypothetical protein	1014	0
39			NP_663788.1	Rho guanine nucleotide exchange factor 7 isoform b; SH3 domain-containing proline-rich protein; PAK-interacting exchange factor beta	1014	0

			BAA04985.1	this sequence overlaps D13631, it covers 9544359 of this sequence.	751	0
		3	XP_042963.2	similar to Rho guanine nucleotide exchange factor 6 (PAK-interacting exchange factor alpha) (Alpha-Pix) (COOL-2)	751	0
			NP_004831.1	Rac/Cdc42 guanine nucleotide exchange factor 6; PAK-interacting exchange factor, alpha; Rac/Cdc42 guanine exchange factor (GEF) 6; rho guanine nucleotide exchange factor 6	751	0
	,		Q15052	ARH6_HUMAN Rho guanine nucleotide exchange factor 6 (PAK-interacting exchange factor alpha) (Alpha-Pix) (COOL-2)	751	0 .
-			AAH39856.1	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	751	0
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \			BAA02796.1	KIAA0006	504	e-142
	,	i	1BY1	A Chain A, Dbl Homology Domain From Beta-Pix	385	e-106
			AAH33768.1	Similar to Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	301	4e-815
NM 009819		U:(C-IR) 2.7			-	
NP_033949.1	U:((Mm.34637 2.71	U:(C-D) 2.71	NP_004380.1	catenin (cadherin-associated protein), alpha 2; Catenin, alpha-2(cadherin-associated protein, related)	1684	0
		·	P26232	CIN2_HUMAN Alpha-2 catenin (Alpha-catenin related protein) (Alpha N-catenin)	1684	0
-			AAA58407.2	cadherin-associated protein-related	1684	0
		,	A45011	alpha-catenin 2	1317	0
:	.;		XP_038221.1	similar to Alpha-1 catenin (Cadherin-associated protein) (AlphaE-catenin)	1317	0
			P35221	CTN1_HUMAN Alpha-1 catenin (Cadherin-associated protein) (Alpha E-catenin)	1317	0
	<u>!</u>		N0607	alpha-catenin 1	1317	0
			BAA02979.1	alpha-catenin	1317	0
	·		AAC99459.1	alphaE-catenin	.1317	0
		:	AAH00385.1	Unknown (protein for MGC:8429)	1317	0
	1	-	BAA03530.1	'human alpha-catenin'	1313	0
•	: :	1	2023176A	alpha catenin	1313	0
		:	JC2542	alpha-2(E)-catenin	1290	0
	.:		AAA18949.1	alpha2(E)-catenin	1290	C

0	0	0 :	0	0	e-107	e-107	e-105	0	183	0	Ó	0	0	0	0	e-136	2e-67	2e-67	2e-67	2e-67	2e-65
1286	1286	974	974	841	389	389	380	3799	3799	3799	3797	2698	2698	786	98/	486	257	257	257	257	250
catenin (cadherin-associated protein), alpha 1, 102kDa; catenin (cadherin-associated protein), alpha 1 (102kD); catenin (cadherin-associated protein), alpha 1 (102kDa	alpha1(E)-catenin	alpha-catenin-like protein	AF091606_1 alphaT-catenin	Similar to catenin (cadherin-associated protein), alpha 2	A Chain A, Alpha-Catenin M-Domain	B Chain B, Alpha-Catenin M-Domain	similar to alpha(E)-catenin	human immunodeficiency virus type I enhancer binding protein 2; human immunodeficiency virus type I enhancer-binding protein 2	HIV-EP2 enhancer-binding protein	MBP-2 (MHC Binding Protein-2)	human immunodeficiency virus type I enhancer-binding protein 2	ZEP2_HUMAN HUMAN IMMUNODEFICIENCY VIRUS TYPE I ENHÄNCER-BINDING PROTEIN 2 (HIV-EP2)	HIV-EP2/Schnurri-2	078779.1 human immunodeficiency virus type I enhancer-binding protein 3	AF278765_1 kappa B and V(D)J recombination signal sequences binding protein	KIAA1555 protein	human immunodeficiency virus type I enhancer binding protein 1; human immunodeficiency virus type I enhancer-binding protein 1	ZEP1_HUMAN Zinc finger protein 40 (Human immunodeficiency virus type I enhancer-binding protein 1) (HIV-EP1) (Major histocompatibility complex binding protein 1) (MBP-1) (Positive regulatory domain II binding factor 1) (PRDII-BF1)	DNA-binding protein PRDII-BF1	PRDII-BF1 protein (AA 1-2717)	DNA-binding protein
NP_001894.1	AAA86430.1	NP_037398.1	AAF21801.1	AAH31262.1	1H6G	1H6G	XP_068797.2	NP_006725.2	WMHUE2	CAA46596.1	AAF81365.1	P31629	AAB88218.1	NP_078779.1	AAK01082.1	BAB13381.1	NP_002105.1	P15822	A34203	CAA35798.1	AAA17534.1
								U:(C-IR) 2.68			* * **					•					T
				4.1				Mm.4215									- 1 - 1 - 2 - 3		****	;	
					1			NM_010437 NP_034567.1		The state of the s										. 1	

			•			
A IC 003777	:	U:(C-IR)				·
•	U.(C-D)	U:(C-D)				
BAB22959.1	Mm.89830	2.18	NP_008950.1	ubiquitin-conjugating enzyme E2C; ubiquitin carrier protein E2-C	343	2e-94
	, ·		000762	UBCC_HUMAN Ubiquitin-conjugating enzyme E2 C (Ubiquitin-protein ligase C) (UbcH10)	343	2e-94
			AAB53362.1	cyclin-selective ubiquitin carrier protein	343	
ĵ.			CAB66118.1	ubiquitin-conjugating enzyme E2 H10 (isoform 1)	343	
			AAH07656.1	ubiquitin carrier protein E2-C	343	<u>.</u>
	·	:	AAH16292.1	ubiquitin-conjugating enzyme E2C	343	2e-94
NM 007511	:					
NP_031537.1	U:(C Mm.87854 2.62	U:(C-IR) 2.62	AAB52902.1	AAB52902.1	2285	
:			NP_000044.1	ATPase, Cu++ transporting, beta polypeptide (Wilson disease); ATPase, Cu++ transporting, beta polypeptide	2282	
		, , , , , , , , , , , , , , , , , , ,	P35670	AT7B_HUMAN Copper-transporting ATPase 2 (Copper pump 2) (Wilson disease-associated protein)	2282	0
			S78555	copper-transporting ATPase (EC 3.6.1) beta	2282	0
•			AAA92667.1	copper transporting ATPase	2282	0
y		4	2001422A	Cu transporting ATPase P	2149	0
			S40525	copper-transporting ATPase (EC 3.6.1) beta chain	2149	0
			Q04656	AT7A_HUMAN Copper-transporting ATPase 1 (Copper pump 1) (Menkes disease-associated protein)	1484	0
			S36149	copper-transporting ATPase (EC 3.6.1) alpha chain	1484	0
			CAB94714.1	Menkes disease	1484	0
2 1			NP_000043.1	ATPase, Cu++ transporting, alpha polypeptide	1484	0
			AAA35580.1	Cu++-transporting P-type ATPase	1484	0
			AAA96010.1	Menkes disease gene	1467	0
			CAB08162.2	CAB08162.2 - Menkes Disease (ATP7A)	1420	0
, , , , , , , , , , , , , , , , , , , ,			AAA79212.1	ORF	1022	0

			AAA16173.1	A16173.1 Wilson disease-associated motein	000	7.17
		11.(C.TR)			SO O	6~I /3
NM_008356		2.61 11:(C-D)		infarfantin 13 recentor alaha 9 areamean interfaction 12 his discommended.		
NP 032382.1	Mm.20855 2.38	2.38	NP_000631.1	13 receptor alpha 2 chain; IL-13 receptor.	431	e-120
	; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;			1132_HUMAN Interleukin-13 receptor alpha-2 chain precursor (Interleukin-13		
:]			Q14627	binding protein)	431	e-120
, 1			CAA64617.1	interleukin 13 receptor	431	e-120
			AAB17170.1	interleukin-13 receptor	431	e-120
			CAA70021.1	IL-13 receptor	431	e-120
			CAD18962.1	dA204F4.1 (interleukin 13 receptor, alpha 2)	431	e-120
			AAH20739.1	interleukin 13 receptor, alpha 2	431	e-120
			AAH33705.1	interleukin 13 receptor, alpha 2	431	85-120 6-120
		U:(C-IR)	AAG17965.1	AF089087_1 G protein-coupled receptor	411	¢-114
1		2.59 TT.(C:T)	,			:
		335	;		·	
NM_022320 Mm.1527 NP_071715.1 80	Mm.1527 80	U:(R-D) 2.3				
	:	,	NP_005292.1	G protein-coupled receptor 35	409	e-113
			09НС97	GP35_HUMAN Probable G protein-coupled receptor GPR35	409	e-113
		·	AAC52028.1	G protein-coupled receptor	409	e-113
	. ,	Ţ				
NM_010174 Mm.2222 NP_034304.1 0	Mm.2222 0	U:(C-IR) 2.54	CAA71305.1	mammary-derived growth inhibitor	241	5e-64
. 1.			NP_004093.1	fatty acid binding protein 3	240	1e-63
			XP_049316.1	similar to Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	240	1e-63
	:	1	P05413	FABH HUMAN Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	240	1e-63
	i ji		FZHUC	fatty acid-binding protein, cardiac and skeletal muscle - human	240	1e-63
:	-					

WO 200	5/08	3239	8					1	186							I	PCT	/US	2 00	5/005	596			
	1e-63	1e-63	1e-63	1e-63	66-63	6e-63	66-63	66-63	86-63-98	1e-62	96-56			0	0	0	0	0	0	2e-54			٠	2e-54
	240	240	240	240	238	238	238	238	238	237	214			1206	1205	1205	1197	1197	1197	209				209
	muscle fatty-acid-binding protein (FABP)	fatty acid binding protein FABP	fatty acid binding protein	AAH07021 fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	A Chain A, Solution Structure Of Human Heart-Type Fatty Acid Binding Protein	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	Fatty Acid Binding Protein (Holo Form, Human Muscle) (M-Fabp)	fatty acid-binding protein	heart fatty acid binding protein; hFABP			cyclin F	CG2F_HUMAN G2/mitotic-specific cyclin F	cyclin F	cyclin F; G2/mitotic-specific cyclin F; F-box only protein 1	cyclin F	cyclin F [Homo sapiens]	lymphocyte antigen 6 complex, locus H				LY6H_HUMAN Lymphocyte antigen Ly-6H precursor
	CAA39889.1	AAB02555.1	AAC99800.1	AAH07021.1	1G5W	1HIMR	1HMS	1HMT	2HIMB	1714345A	AAB29294.1	•	\ .	AAB60342.1	P41002	AAH12349.1	NP_001752.1	A55501	CAA85308.1	NP_002338.1				094772
						1		1 3 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		1		U:(C-IR)	2.52 U:(C-D)	2.12		***				U:(C-IR)	U.(C-D)	7.09 U:(RD)	2.06	
• ,			÷			:								Mm.4008	1				,			Mm.2215	4	
				, ,									NM_00/634	NP_031660.1							, , ,	NM_011837	-NP_035967.1	

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	2e-54	2e-54	2e-54	0	٠	ļ.º	0	0	0	0	0	e-180	e-111	e-1111	e-111	e-111	e-111	e-111	2e-96			0	
	209	209	209	2207		2207	2207	2202	2202	1523	687	. 630	402	402	402	402	402	402	353			1257	1057
		1 lymphocyte antigen 6 complex, locus H	1 lymphocyte antigen 6 complex, locus H	CFTR_HUMAN Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel)		cystic fibrosis transmembrane conductance regulator			cystic fibrosis transmembrane conductance regulator		cystic fibrosis transmembrane conductance regulator	coded for by human cDNA M96936 (NID:g180293)	1 Similar to ATP-binding cassette, sub-family C (CFTR/MRP), member 4	1 ATP-binding cassette protein C4 splice variant A	multidrug resistance-associated protein	1 ATP-binding cassette, sub-family C, member 4; canalicular multispecific organic anion transporter (ABC superfamily)	MRP4_HUMAN Multidrug resistance-associated protein 4 (MRP/cMOAT-related ABC transporter) (Multi-specific organic anion transporter-B) (MOAT-B)	ABC transporter MOAT-B	ABC transporter MOAT-B isoform			•	CARE_HUMAN Caspase recruitment domain protein 14 (CARD-containing MAGHK protein
DA 42/115 1	DAA54115.1	AAH28894.1	AAH30192.1	P13569		DVHUCF.	AAC13657.1	NP_000483.2	AAA35680.1	AAB46352.1	AAB46340.1	AAB46341.1	AAH41560.1	AAN17334.1	AAL88745.1	NP_005836.1	015439	AAC27076.1	AAC27077.1			NP_077015.1	O9BXI.6
				U:(C-IR) 2.5	U:(C-D) 2.36						٠							*		U:(C-IR)	U:(C-D)	2.33	
					Mm.1562 1				7												Mm.13083	7	
,			,		NM_021050 NP_066388.1			1.54. 1.54.												A E 2 6 3 1 5 7		AAK6013/.1	

1257	953 0 407 e-113
	RD-containing
	Similar to caspase recruitment domain protein 14 caspase recruitment domain protein 14 isoform 2; CARD-containing
2 protein	Similar to caspase recruitment domain protein 14 caspase recruitment domain protein 14 isoform 2;
AF322642_1 caspase recruitment domain protein 14 CARD-containing MAGUK 2 protein	spase recruitmen itment domain p
AF322042_1 CARD-contain	Similar to caspa caspase recruit
_	438170.1
AA	AAI
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U5/U8 <i>23</i>	<u>.</u>						189)								C1/	USZ	เบบอ	/003	5596		
e-128	e-128	e-128	e-128	a 101	e-119	e-116	0	0	0	4e-63										e-169	e-169	e-169
456	456	456	455	727	428	418	891	891	891	241				,						595	595	595
solute carrier family 22 member 6 isoform a; renal organic anion transporter 1; para-aminohippurate transporter	hOAT1-1	organic anion transporter	para-aminohippurate transporter	NP_700357.1 urate anion exchanger 1 isoform b; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12			KIAA0737 gene product	KIAA0737 protein	AAH13689 KIAA0737 gene product	similar to CAGF9										FRZB_HUMAN Frizzled-related protein precursor (Frzb-1) (Frezzled) (Fritz)	frezzled	Unknown (protein for MGC:34598)
NP 004781.2	BAA75072.1	CAB77184.1	AAD10052.1	 NP 700357.1	 NP_695011.1	BAB47393.1	NP_055643.1	BAA34457.1	AAH13689.1	XP_049037.5		·			,	,			:	092765	AAC51217.1	AAH27855.1
							U:(C-IR) 2.47				·		·			1	-			U:(C-IR) 2.45		
						-	Mm.2855 3				,									Mm.3246		
					21		NM_023434 · NP_075923.1								,			: .		NM_011356 NP_035486.1		

e-169	e-169	e-169	2e-84	2e-84	0	0		0	190	e-152	e-152	e-151	e-151	e-151	e-150	e-150	e-149	e-149	e-149	e-148	e-148	e-148	2e-71	2e-71
593	593	593	312	312	1033	1033		1033	1033	536	535	534	534	532	531	530	526	526	526	573	523	523	268	268
frizzled-related protein; Fritz; Frzb-1; fre; frizzled (Drosophila) homolog-related; fzrb; hffz	Frzb precursor	Fritz	secreted frizzled-related protein 4; secreted frizzled-related protein 4	fipHE	acyl-Coenzyme A oxidase 2, branched chain; Peroxisomal branched chain acyl-CoA oxidase	CAO2_HUMAN Acyl-coenzyme A oxidase 2, peroxisomal (Branched-chain acyl-CoA oxidase) (BRCACox) (Trihydroxycoprostanoyl-CoA oxidase) (THCCox)	(THCA-CoA oxidase)	branched chain acyl-CoA oxidase	peroxisomal branched chain acyl-CoA oxidase	peroxisomal acyl-coenzyme A oxidase	CAO1_HUMAN Acyl-coenzyme A oxidase 1, peroxisomal (Palmitoyl-CoA oxidase) (AOX)	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal	peroxisomal acyl-CoA oxidase	AAH08767 Similar to acyl-Coenzyme A oxidase 1, palmitoyl	AAH10425 Unknown (protein for MGC:15225)	peroxisomal fatty acyl-coA oxidase	acyl-Coenzyme A oxidase isoform b; acyl-coenzyme A oxidase 1,	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form I		acyl-Coenzyme A oxidase isoform a; acyl-coenzyme A oxidase 1	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form II	acyl-CoA oxidase	acyl-Coenzyme A oxidase 3, pristanoyl	CAO3_HUMAN Acyl-coenzyme A oxidase 3, peroxisomal (Pristanoyl-CoA oxidase)
NP_001454.1	AAC50736.1	AAB51298.1	NP_003005.1	AAC04617.1	NP_003491.1	Q99424	•	CAA64489.1	CAB65596.1	AAB30019.2	Q15067	I38095	CAA50574.1	AAH08767.1	AAH10425.1	AAA18595.1	NP 009223.1	A54942	AAA19113.1	NP 004026.1	B54942	AAA19114.1	NP_003492.1	015254
-				V	U:(C-IR) 2.42						ì			; ² .					:					S .
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			1.	,	NM_053115 NP_444345.1							. ,.												

			r			
			CAA72214.1	pristanoyl-CoA oxidase	268	17 oc.
,	,	U:(C-IR) 2.42	NP_001731.1	calbindin 2 full length protein isoform; calbindin 2, (29kD, calretinin); calbindin D29K	371	e-102
	÷		P22676	CLB2_HUMAN Calretinin (CR) (29 kDa calbindin)	371	100
			A60253	calretinin	371	6-102
٠.			CAA39991.1	calretinin	377	102
			1709139B	calretinin	371	e-102
			AAH15484.1	AAH15484 calbindin 2, (29kD, calretinin)	371	e-102
,	:		NP 004920.1	calbindin 1; calbindin 1, (28kD)	249	99-e5
	-	-	P05937	CABV_HUMAN Calbindin (Vitamin D-dependent calcium-binding protein, avian-type) (Calbindin D28) (D-28K)	249	5e-66
		·	S00234	calcium-binding protein, vitamin D-dependent	249	191 29-95
			CAA29860.1	calbindin (AA 1-261)	249	5e-66
			AAC62230.1	27kDa calbindin	240	5 - 66
	•:			calbindin 1	240	20-00
,		•	AAH06478.1	AAH06478 calbindin 1, (28kD)	249	26-66
		1	AAH20864.1	AAH20864 calbindin 1, (28kD)	249	5e-66
		1. 2.	1403296A	calbindin 27kD	249	5e-66
			1709139A	calbindin D28K	249	56-66
		•	NP_009019.1	calbindin 2 isoform 22k; calbindin 2, (29kD, calretinin); calbindin D29K	199	1e-50
		,	NP_009018.1	009018.1 calbindin 2 isoform 20k; calbindin 2, (29kD, calretinin); calbindin D29K	198	16-50
NM_013612 NP_038640.1	Mm.2913	U:(C-IR) 2.38	XP_002585.4	similar to Natural resistance-associated macrophage protein 1 (NRAMP 1)	905	0
			P49279	NRM1_HUMAN Natural resistance-associated macrophage protein 1 (NRAMP 1)	905	0
· ·			155679	integral membrane protein	905	0
		1.4.	AAA57521.1	integral membrane protein	905	0
			BAA08908.1	Nramp	905	0
			AAG15405.1	natural resistance-associated macrophage protein 1	905	0
	1				3	>

	904 0	0 688	s), member 1; 887 0 imaniasis);	887 0		0 649	649	649	0		transporters), 649 0	NRAMP 2) 648 0	648	. 648 0	648 0	633 0	629 e-180		260	092		
Nrama	drum	natural resistance-associated macrophage protein NRAMP 1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1; natural resistance-associated macrophage protein 1 (might include Leishmaniasis); solute carrier family 11 (sodium/phosphate symporters), member 1	NRAMP	Nramp	divalent metal transporter	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2; natural resistance-associated macrophage protein 2	NRAMP2	natural resistance-associated macrophage protein 2	NRAMP2 iron transporter	AAH02592 solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	NRM2_HUMAN Natural resistance-associated macrophage protein 2 (NRAMP 2) (Divalent metal transporter 1) (DMT1)	natural resistance-associated macrophage protein 2 non-IRE form	natural resistance-associated macrophage protein 2	natural resistance-associated macrophage protein 2 non-IRE form	natural resistance-associated macrophage protein 2	integral membrane protein	integral membrane protein	taste receptor T2R1; taste receptor, family B, member 7; taste receptor, type 2, member 1	AF227129_1 candidate taste receptor T2R1	unnamed protein product	
BAA08907 1	1000	-	NP_000569.1	CAA57541.1	BAA07370.1	CAD38517.1	NP_000608.1	BAA24933.1	AAC21460.1	AAC18078.1	AAH02592.1	P49281	AAC21459.1	AAC21461.1	BAB93467.1	BAA34374.1	157022	AAA79219.1	NP_062545.1	AAF43902.1	BAB14854.1	
				7 : 5 :										1.	-			,	U:(C-IR) 2.38	,	U:(C-IR) 2.36	
						•				,			:						Mm.1038 03		Mm.2771	
,							-												NM_020503 NP_065249.1		NM_026091 NP_080367.1	

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	4e-88	4e-88	1e-87	1e-87				0	. 0	0	0	8e-91	8e-91	8e-91	86-91	2e-83	2e-83	2e-83	2e-83	2e-83	2e-83	26-83	4e-75	4e-75
	323	323	321	321			629	629	673	673	673	332	332	332	332	308	308	308	308	308	308	308	780	280
AAH19196 Unlmown (mootsin for MCC 4240)		cmonosome 20 open reading frame 27	chromosome 20 open reading frame 27	unnamed protein product			CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)	AF217524_1 gap junction protein alpha 8	gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)	intrinsic membrane protein MP70	gap junction membrane channel protein alpha-	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)	bA264J4.3 (novel connexin (gap junction protein))	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)	gap-junction protein alpha 3	gap junction protein, alpha 5, 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)	connexin 40	AF151979_1 connexin 40	connexin40	AAH13313 gap junction protein, alpha 5, 40kD (connexin 40)8	connexin40	AF271261_1 connexin 58	connexin 59; gap junction alpha 10
AAH121961	A A TTO A00 C 1	AAH24030.1	NP_060344.1	BAA91252.1			P48165	AAF32309.1	NP_005258.1	139176	AAA77062.1	NP_068773.2	CAC16957.1	09У6Н8	AAD42925.1	NP_005257.2	P36382	AAA91833.1	AAD37801.1	AAA60457.2	AAH13313.1	138429	AAK55516.1	NP_110399.1
,			.				U:(C-IR) 2.35	4	-															
				-	;		U:(C-IR) Mm.56907 2.35							i .				,				* 4		
					:	NM 008123	1					; ;												

			:			
			P57773	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)	280	4e-75
			AAG09406.1	AF179597_1 connexin 59	280	4e-75
			NP_115991.1	connexin 62	279	8e-75
			AAK51676.1	AF296766_1 connexin 62	279	8e-75
			CAC93847.1	connexin62	279	8e-75
			AAD56533.1	AF180815_1 truncated connexin 37 polymorph	267	3e-71
NM_013473 NP_038501.2	Mm.3267	U:(C-IR) 2.35	XP_036593.2	similar to annexin A8	296	e-170
		,	AAH04376.1	AAH04376 annexin A8	596	e-170
			NP_001621.1	annexin VIII; Annexin VII	595	e-169
	.1 '		P13928	ANX8_HUMAN Annexin A8 (Annexin VIII) (Vascular anticoagulant-beta) (VAC-beta)	595	e-169
			CAA34650.1	vascular anticoagulant-beta (AA 1 - 327)	595	e-169
			LUHU8	amexin VIII	593	e-169
•		·	AAB46383.1	anexin VIII	590	e-168
•	,		XP_054475.4	similar to annexin A8	575	e-165
			P09525	ANX4_HUMAN Annexin A4 (Annexin IV) (Lipocortin IV) (Endonexin I) (Chromobindin 4) (Protein II) (P32.5) (Placental anticoagulant protein II) (PAP-II) (PP4-X) (35-beta calcimedin) (Carbohydrafe-binding protein P33/P41) (P33/41)	337	4e-92
·			NP_001144.1	annexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
,			XP_031596.2	similar to annexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
			A42077	amexin IV	337	4e-92
			AAA51740.1	annexin IV (placental anticoagulant protein II)	337	4e-92
				annexin IV (carbohydrtate-binding protein p33/41)	337	4e-92
			AAH00182.1	AAH00182 annexin A4	337	4e-92
			AAH11659.1	AAH11659 Similar to annexin A4	337	4e-92
			AAC41689.1	protein PP4-X	337	4e-92

									19													
00 %	20-02	76-87	,					0 0) C	0	130	26-123	2e-85	2e-85	Ze-85	2e-85	1e-84	2e-82	26-87	2e-82	2e-81
308	220	970	. 281	001	001	991	100	034	450	652	652	450	315	315	315	315	315	312	305	305	305	302
calphobindin	coagulation inhibitor		gamma-aminobutyric acid (GABA) receptor, rho 1; gamma-aminobutyric acid (GABA) A receptor, rho-1	GAR1_HUMAN Gamma-aminobutyric-acid receptor rho-1 subunit precursor (GABA(A) receptor)	gamma-aminobutyric acid receptor A rho-1 chain precursor		GAR2_HUMAN Gamma-aminobutyric-acid receptor rho-2 subunit precursor (GABA(A) recentor)		1			similar to Gamma-aminobutyric-acid receptor rho-3 subunit precursor (GABA(A) receptor)		· i	 (GABA(A) receptor)	gamma-aminobutyric acid A receptor beta 3 chain splice form 1	GABA-alpha receptor beta-3 subunit	gamma-aminobutyric acid (GABA) A receptor, beta 3		GAD_HUMAN Gamma-aminobutyric-acid receptor delta subunit precursor (GABA(A) receptor)		gamma-aminobutyric acid (GABA) A receptor, delta
1512315A	1313303A		NP_002033.1	P24046	A38627	AAA52509.1	P28476	CAC07339.1	NP_002034.1	A38079	AAA52510.1	XP 116036.2	NP_068712.1	NP_000805.1	F28472	A55275	AAA52511.1	AAH10641.1	NP_000806.1	014764	AAB70007.1	AAH33801.1
	1	·	U:(C-IR) 2.33	•					,			•			 . [1.7	;		: · ·	
			Mm.14116	1					<i>.</i>					á			1					
	ţ	NM_008075	U:(C NP_032101.1 Mm.14116 2.33													, V	2			,		

	1 .		•		:	
			NP_000804.1	gamma-aminobutyric acid (GABA) A receptor, beta 2, isoform 2	302	2e-81
			P47870	GAB2_HUMAN Gamma-aminobutyric-acid receptor beta-2 subunit precursor (GABA(A) receptor)	302	2e-81
			AAB29370.1	gamma-aminobutyric acid A receptor beta 2 subunit; (GABA)A receptor beta 2 subunit	302	2e-81
			AAB33983.1	GABAA receptor beta 2 subunit	302	.2e-81
00800 MN	` .	TT.(C.TR)				
NP_032035.1	Mm.46053 2.32	2.32	NP_005121.1	heparin-binding growth factor binding protein	268	2e-71
			A41178	heparin-binding growth factor-binding protein precurso	268	2e-71
	`		AAA58636.1	heparin binding protein	268	2e-71
-			AAD39216.1	AF149412_1 HBP17 heparin-binding and FGF-binding protein	268	. 2e-71
			AAH03628.1	heparin-binding growth factor binding protein	268	7e-71
		. '	AAH08910.1	heparin-binding growth factor binding protein	268	2e-71
NM_008352		U:(C-IR) 2.29 U:(C-D)		interleukin 12B precursor; natural killer cell stimulatory factor-2; interleukin 12B; cytotoxic lymphocyte maturation factor 2, n40; interkenkin-12 beta chain: interleukin		
NP_032378.1		2.24	NP_002178.2	12, p40; natural killer cell stimulatory factor, 40 kD subunit, IL23, subunit p40	431	e-120
			P29460	I12B_HUMAN Interleukin-12 beta chain precursor (IL-12B) (Cytotoxic lymphocyte maturation factor 40 kDa subunit) (CLMF p40) (NK cell stimulatory factor chain 2) (NKSF2)	431	e-120
,			A38957	interleukin 12B precursor	431	e-120
			AAA35695.1	cytotoxic lymphocyte maturation factor 40 kDa subunit	431	e-120
,	1		AAD56386.1	AF180563_1 interleukin 12, P40	431	e-120
,			AAG32620.1	interleukin 12 p40 subunit	431	e-120
	-		A A 1 (2 / 170) 1	AF\$12686_1 interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic	121	120
			1,201-CMAA	1) III) III) Color III anni anni anni 2, p-0)	£ 5	071-0
			AAA59938.1	natural killer cell stimulatory factor	429	e-120
\frac{1}{2}	:		1F42	A Chain A, The P40 Domain Of Human Interleukin-12	400	e-111
			1F45	A Chain A, Human Interleukin-12	400	e-1111

5e-61		3e-56
234		178
B32547.1 small integral membrane protein of lysosome/late endosome		004853.1 LPS-induced TNF-alpha factor
BAB32547.1		NP 004853.1
U:(C-IR) BAE 2.28	U:(C-D) 2.11	
	Mm.2111 9	
: :	NM_019980 NP_064364.1	

3e-56	20 56	22.50	26-20			70-91		2e-62	2e-62	20,67	20-02	2e-62	2e-61	2e-61	2e-61		28-61	26-61	20.61	66-53	5e-88	5e-88
178	178	170	7/0	ŀ	020	667		238	238	738	238	238	235	235	235		235	235	235	207	186	186
LITF_HUMAN Lipopolysaccharide-induced tumor necrosis factor-alpha factor (LPS-induced TNF-alpha factor) (P53-induced protein 7)	LPS-Induced TNF-Alpha Factor	Pig7			teratocarcinoma-derived growth factor 1				CRII_HUMAN Teratocarcinoma-derived growth factor 1 (Epidernal growth factor-like cripto protein CR1) (Cripto-1 growth factor) (CRGF)	teratocarcinoma-derived growth factor 1	cripto protein (AA 1-188)	teratocarcinoma-derived growth factor 1	CRI2_HUMAN Teratocarcinoma-derived growth factor 2 (Epidermal growth factor-like cripto protein CR3) (Cripto-3 growth factor)	teratocarcinoma-derived growth factor 3	EGF repeat containing protein; HUMTDGF1A Human (clone CR)	teratocarcinoma-derived growth factor 1 (TDGF1) gene P13385; coded for by human cDNAs M96956 (NID:g339432), X14253 (NID:g30220) and M96955 (NID:g339430)	AF251549_1 cripto 3	AF251550_1 cripto 3	teratocarcinoma-derived growth factor	092153.1 similar to teratocarcinoma-derived growth factor 1	similar to acyl-malonyl condensing enzyme	689675.1 hypothetical protein FLJ40154
Q99732	AAB36550.1	AAC39530.1	, .		AAH22393.1	• -		NF_005203.1	P13385	A30362	CAA32467.1	AAA61134.1	P51864	AAA61135.1	AAB46353.1		AAG49538.1	AAG49539.1	A39787	XP_092153.1	XP_083967.1	NP 689675.1
t .				:	U:(C-IR)	2.28 U:(C-D)	60.7								-		3				U:(C-IR) 2.27	1
						Mm 5090				,		•				-					Mm.6211	
		: 1	•		. '	NM_011562 NP_0356921	1.70000 11				4						;				NM_019871 NP_063924.1	

		BAC05067 1	the many own distribution of the second of t		
		T. 093050 TA	┓.	186	5e-88
	1	AF_0055900.2	similar to acyl-maionyl condensing enzyme	184	2e-87
		INF 4/5509.1	ALT 4/3309.1 acyl-maionyl condensing enzyme	182	. 2e-85
	1	CAC82744.1	acyl-malonyl condensing enzyme	182	2e-85
		XP_064583.3	similar to acyl-malonyl condensing enzyme	183	L
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059620 MN	U:(C-IR)	I 👝	AVA2 HTIMAN A Istings and Languages 2 (P. 1).		
D:(C NP 033780.1 Mm.87748 2.43	U:(C-D)	075969	3)(PRKA3) (A-kinase anchor protein 110 kDa) (AKAP 110) (Sperm oocyte binding protein) (Fibrousheathin I) (Fibrous sheath protein of 95 kDa) (FSP95	1170	0
		AAC63371.1	protein kinase A binding protein AKAP110	1170	0
·		AAD21218.1	sperm oocyte binding protein	1167	0
		NP 006413.2	kinase (PRKA) anchor protein 3; sperm oocyte binding protein 1; fibrousheathin 1	1167	
		AAC35854.1	fibrousheathin I	1163	0
		NP_647450.1	kinase (PRKA) anchor protein 4 isoform 2; A-kinase anchor protein 82 kd	375	e-103
		NP_003877.2	A kinase (PRKA) anchor protein 4 isoform 1; A-kinase anchor protein 82 kDa	375	e-103
		AAC79433.1	major sperm fibrous sheath protein precursor	371	e-102
	`	CAA75494.1	sperm protein	270	1e-72
	•	JC5986	A-kinase anchoring protein homolog	264	76-71
NM_008166					11/2/
NP 032192.1 Mm.7983	U:(C-IR) 3 2.26) BAA86534.1	KIAA1220 protein	1405	
		XP_043613.7	similar to glutamate receptor delta-1 subunit	1379	
	•	,			,

			AAH39263.1	Similar to glutamate receptor, ionotropic, delta 1	1202	6
	,		NP_001501.1	glutamate receptor, ionotropic, delta 2; GluR-delta-2	1141	0
			043424	GRD2_HUMAN Glutamate receptor delta-2 subunit precursor	1141	C
			AAC39579.1	glutamate receptor delta-2 subunit	1141	0
			NP_000821.1	glutamate receptor, ionotropic, kainate 1; human glutamate receptor (GLUR5)	362	2e-99
			P39086	GLK1_HUMAN Glutamate receptor, ionotropic kainate 1 precursor (Glutamate receptor 5) (GluR-5) (GluR-5) (GluR-5) (GluR-5)	362	2e-99
1			158178	glutamate receptor	362	2e-99
			AAA52568.1	glutamate receptor	362	2e-99
·		:	CAC80546.1	glutamate receptor subunit GluR5	359	1e-98
			AAA95961.1	EAA3	357	8e-98
			CAC80548.1	glutamate/kainate receptor subtype GluR7	346	16-94
			NP_000822.1	glutamate receptor, ionotropic, kainate 3	344	5e-94
			AAB60407.1	EAA5	344	5e-94
NM_011427 NP_035557.1	I Mm.2093	U:(C-IR) 2.26	AAD17332.1	zinc finger protein	442	e-124
			NP 005976.2	snail 1 homolog; snail 1 zinc finger protein	442	e-124
			095863	SNAI HUMAN Zinc finger protein SNAI1 (Snail protein homolog) (Sna protein)	442	e-124
	1		CAB52414.1	SNAI1 protein	442	e-124
			AAD52986.1	AF155233_1 snail zinc finger protein	442	e-124
	9 (CAC07340.1	dJ710H13.1 (snail 1 (drosophila homolog), zinc finger protein)	442	e-124
			AAH12910.1	AAH12910 Unknown (protein for MGC:21748)	- 442	e-124
`.			XP_065615.1	similar to snail 1 (drosophila homolog), zinc finger protein	355	1e-97
			AAF32527.1	AF131208 1 snail protein	250	3e-66
			NP_003059.1	snail 2; neural crest transcription factor SLUG; slug (chicken homolog), zinc finger protein	249	99-99
			043623	SLUG_HUMAN Zinc finger protein SLUG (Neural crest transcription factor Slug) (Snail homolog 2)	249	99-99
			AAC34288.1	zinc finger protein slug	249	99-99

[9	श्र	99	34	T ?	4° ·	,	<u>4</u>	<u> </u>	202 ∞	2		œ	150	15	Ϊ́	1 55	T	Т	T	Ť		: :	1 =	1 7
L	99-99	99-99	99-99	e-134		e-134		e-134	e-110	2e-98			2e-98	3e-67	3e-67	7e-50	9e-53		:			0p_51	9e-51	0p-51	
3,0	249	249	249	477	377	, ,		475	397	358			358	254	254	196	206					183	182	183	102
55240.1 AF084243 1 zinc finger protein QT 172	Т			AF409141_1 NIP1	1 amyloid beta (A4) precursor protein-hinding family A member 2 hinding anotesin		interacting protein 2; neuronal calcium-binding protein NECAB3	Ţ,			isoform 2; synaptotagmin interacting protein STIP3; X11L-binding protein 51; amyloid beta (A4) precursor protein-binding, family A, member 2; synaptotagmin	interacting protein 2; neuronal calcium-binding protein NECAB3		synaptotagmin interacting protein 1	unnamed protein product	AF193756_1 neuronal calcium binding protein NECAB1	PNG gene					MARK4 serine/threonine protein kinase	unnamed protein product	MAP/microtubule affinity-regulating kinase-like 1	_
AAD55240.1	A AH14800 1	1,124,200,1	AAH13895.1	AAL01118.1	NP 112508.1	I	-	AAG28415.1	CAD37360.1	NP_112509.1			BAB16413.1	NP 071746.1	BAC04568.1	AAG28412.1	2208307A					AAL23683.1	BAC11510.1	AAM55491.1	BAC033751
				U:(C-IR) 2.26				•									U:(C-IR) 2.24		1			U:(С-ІК) 2.23			
			┰	Mm.1437 48			,		-						!		Mm.4614 2					Mm.29522			
				NM_021546 NP_067521.1							2.		:				NM_025746 NP_080022.1			1	AK010751	AAN60072.1			

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(9e-51 e-144	e-143	e-143	e-143	e-143	e-143	e-128	1e-90	1e-90	3e-80	1e-70	1e-70	4e-67	96-67	9e-67	79-96		0
100,	508	506	206	506	506	206	458	332	332	298	266	266	254	253	253	253		1038
unnamed protein product		beta-1,3-N-acetylglucosaminyltransferase bGnT-3; type II membrane protein; transmembrane protein 3; core 1 extending beta-1,3-N-acetylglucosaminyltransferase; beta-1,3-galactosyltransferase; beta-1,3-galase 8; beta3gal-T8; UDP-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase 8; beta-3-GX-T8	B3G8_HUMAN Beta-1,3-galactosyltransferase 8 (Beta-1,3-GalTase 8) (Beta3Gal-T8) (b3Gal-T8) (UDP-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase 8) (UDP-Gal:beta-GlcNAc beta-1,3-galactosyltransferase 8) (Beta-3-Gx-T8) (Core 1 extending beta-1,3-N-acetylglucosaminyltransferase) (Core1-beta3GlcNAcT)	type II membrane protein	AF293973_1 core 1 extending beta-1,3-N-acetylglucosaminyltransferase	beta-1,3-galactosyltransferase	beta 1,6-GlcNAc-transferase	beta-1,3-N-acetylglucosaminyltransferase protein	beta-1,3-N-acetylglucosaminyltransferase 6	Unknown (protein for IMAGE:4907098)	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7; hypothetical gene supported by AK000770	AF502430_1 beta 1,3-N-acetylglucosaminyltransferase 7	beta-1,3-galactosyltransferase	unnamed protein product	beta 1,3 galactosyltransferase	AF321825_1 beta-1,3-galactosyltransferase-related protein		neutrophil lactoferrin
BAB55238.1	BAB21531.1	NP_055071.1	Q9Y2A9	BAA76497.1	AAK00849.1	CAC45044.1	CAC82374.1	NP 619651.1	BAB88882.1	AAH25357.1	NP_660279.1	AAM61770.1	CAC45045.1	BAC04622.1	CAC82375.1	AAL37219.1	io.	AAA59479.1
	U:(C-IR) 2.22 U:(C-IR) 2.41						4.								,			U:(C-IR) 2.22
	Mm.2885 6			,	. ; '	ţ				e.								- 1
	NM_028189 NP_082465.1						3								-		NM_008522	NP 032548.1 Mm.7612

			000000	TRFL_HUMAN Lactotransferrin precursor (Lactoferrin) [Contains: Lactoferroxin A;		
			FU2/00	Lactorenoxin B; Lactorenoxin C	1038	0
			TFHUL	lactotransferrin precursor	1038	0
	.i.	·	AAB60324.1	lactoferrin	1038	6
			AAH15822.1	lactotransferrin	1036	C
			AAH22347.1	lactotransferrin	1035	0
			CAA37116.1	precursor lactoferrin (709 AA)	1035	O
			AAA36159.1	lactoferrin	1035	C
	14.7		AAN11304.1	lactoferrin	1035	0
			AAA59511.1	lactoferrin	1035	0
		:	AAG48753.1	lactoferrin precursor	1034	
			AAN63998.1	lactotransferrin precursor	1034	04
			AAH15823.1	lactotransferrin	1033	0
			NP_002334.1	002334.1 lactotransferrin	1032	0
; •		•	CAA37914.1	CAA37914.1 precursor (AA -19 to 692)	1032) C
NM_009637					7001	
NP_033767.1	U:((Mm.86453 2.22	U:(C-IR) 2.22	XP_058567.1	similar to AE binding protein 2; AE-binding protein 2	263	. 160
			NP 694939.1	hypothetical protein MGC17922	563	160
			AAH15624.1	AAH15624 Similar to AB-binding protein 2	562	e-160
, ,	·		AAH22220.1	Unknown (protein for MGC:17922)	562	e-160
NM_010198 NP_034328.1	Mm.5723 8	U:(C-IR) 2.22	NP_004103.1	fibroblast growth factor 11; fibroblast growth factor homologous factor 3	444	e-125
	·	,	092914	FGFB_HUMAN Fibroblast growth factor-11 (FGF-11) (Fibroblast growth factor homologous factor 3) (FHF-3)	444	e-125
			AAB18915.1	fibroblast growth factor homologous factor 3	444	e-125
			AAL15439.1	fibroblast growth factor 11	444	e-125
		:	AAM11871.1	fibroblast growth factor 11	444	e-125
	,		AAH32502.1	fibroblast growth factor 11	444	e-125

NP 004106.1 Broblest growth factor 14, fibroblast growth factor 14, fibroblast growth factor 14 (FGF-14) (Fibroblast growth factor 15 fibroblast growth factor 14 (FGF-14) (Fibroblast growth factor 15 fibroblast growth factor homologous factor 15 fibroblast growth factor 12 isofom 1, fibroblast growth factor 1, 273 26-73 (AAB18913.1 fibroblast growth factor 10 (FGF-12) (Fibroblast growth factor 1, 273 26-73 (AAB18913.1 fibroblast growth factor 11 (FGF-12) (Fibroblast growth factor 1, 273 26-73 (AAB18913.1 fibroblast growth factor 11 (FGF-13) (Fibroblast growth factor 1, 273 26-73 (AAB18913.1 fibroblast growth factor 11 (FGF-13) (Fibroblast growth factor 1, 273 26-53 (AAB18913.1 fibroblast growth factor 13 isofom 1A; fibroblast growth factor 1, 274 246 26-65 (AAB18914.1 fibroblast growth factor 13 isofom 1A (FGF-13) (Fibroblast growth factor 13 isofom 12 ifroblast growth factor 13 isofom 14 isofom 15 is							
FIGHE HUMAN Fibroblast growth factor-14 (FGF-14) (Fibroblast growth factor 273 homologous factor 4) (FHF-4) 318916.1 fibroblast growth factor homologous factor 1, 273 106025.1 fibroblast growth factor 12 isoform 1; fibroblast growth factor 1, 273 1060360.1 fibroblast growth factor 12 isoform 1; fibroblast growth factor 1, 273 1060360.1 fibroblast growth factor 12 isoform 1, fibroblast growth factor 1, 273 1060360.1 fibroblast growth factor 1, 273 1060360.1 fibroblast growth factor 1, 273 11801.2 FGFC_HUMAN Fibroblast growth factor 1 (FGF-12) (Fibroblast growth factor 1, 273 11801.3 fibroblast growth factor 1, 3, isoform 1A, fibroblast growth factor 1 (FGF-13) (Fibroblast growth factor 1, 3, isoform 1A, fibroblast growth factor 1, 246 11801.1 fibroblast growth factor 13 isoform 1A 11801.2 fibroblast growth factor 13 isoform 1A 11801.1 fibroblast growth factor 13 isoform 2, fibroblast growth factor 1, 223 11801.2 fibroblast growth factor 1 isoform 1, 223 11802.2 fibroblast growth factor 1 isoform 1B, fibroblast growth factor 1 isoform 1B 118786.3 fibroblast growth factor 13 isoform 1B 118786.1 fibroblast growth factor 13 isoform 1B					fibroblast growth factor 14; fibroblast growth factor homologous factor 4	273	16.73
18916.1 fibroblast growth factor homologous factor 4 273 18025.1 AE014303 1 FHF4 273 18025.1 fibroblast growth factor 12 isoform 1; fibroblast growth factor 12 isoform 1; fibroblast growth factor 1 fibroblast growth f) 2		,	Q92915	FGFE_HUMAN Fibroblast growth factor-14 (FGF-14) (Fibroblast growth factor homologous factor 4) (FHF-4)	273	1e-73
N16025.1 AE014303 1 FHF4 D66360.1 fibroblast growth factor 12 isoform 1; fibroblast growth factor homologous factor 1; 273 myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor 273 homologous factor 1) (FHF-1) (Myocyte-activating factor) FGFC_HUMAN Fibroblast growth factor 12 (FGF-12) (Fibroblast growth factor 1) (FHF-1) (Myocyte-activating factor) 18913.1 fibroblast growth factor 13 isoform 1A; fibroblast growth factor 13 isoform 1A; fibroblast growth factor 13 isoform 1A; fibroblast growth factor 13 isoform 1A homologous factor 2) (FHF-2) (Fibroblast growth factor 13 isoform 1A homologous factor 13 isoform 1B fibroblast growth factor - human FGF-12b fibroblast growth factor - human factor homologous factor 1; 122524.1 Unknown (protein for MGC:26659) 1893 fibroblast growth factor - human factor homologous factor 2 213 fibroblast growth factor 13 isoform 1B fibroblast growth factor 13 isoform 1B fibroblast growth factor 13 isoform 1B				AAB18916.1	fibroblast growth factor homologous factor 4	273	1e-73
1966360.1 fibroblast growth factor 12 isoform 1; fibroblast growth factor 11; fibroblast growth factor 12 isoform 1; fibroblast growth factor 12 fibroblast growth factor 12 fibroblast growth factor 12 fibroblast growth factor 12 fibroblast growth factor 13 fibroblast growth factor 13 fibroblast growth factor 11 fibroblast growth factor 11 fibroblast growth factor 13 isoform 1A; fibroblast growth factor 13 isoform 1A fibroblast growth factor 12 isoform 2; fibroblast growth factor 12 isoform 18; fibroblast growth factor 12 isoform 18; fibroblast growth factor 13 isoform 18; fibroblast growth factor 13 isoform 18 f				AAN16025.1	AE014303_1 FHF4	.273	1e-73
FGFC_HUMAN Fibroblast growth factor-12 (FGF-12) (Fibroblast growth factor 1) (FHF-1) (Myocyte-activating factor) 18913.1 fibroblast growth factor homologous factor 1 18913.1 fibroblast growth factor homologous factor 1 1004105.1 fibroblast growth factor 13, isoform 1A; fibroblast growth factor 13, isoform 1A; fibroblast growth factor 13, isoform 1A; fibroblast growth factor 13 (FGF-13) (Fibroblast growth factor 13, feff-2) 18914.1 fibroblast growth factor 13 isoform 1A 112347.1 fibroblast growth factor 12 isoform 2, fibroblast growth factor 1 isoform 2 isofor					fibroblast growth factor 12 isoform 1; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	273	2e-73
18913.1 fibroblast growth factor homologous factor 1 194239.1 fibroblast growth factor 13, isoform 1A; fibroblast growth factor 13, isoform 1A; fibroblast growth factor 2 246 1913 FGFD_HUMAN Fibroblast growth factor 13 (FGF-13) (Fibroblast growth factor 2 246 18914.1 fibroblast growth factor 13 isoform 1A 112347.1 AAH12347 Unknown (protein for MGC;20109) 1346400.1 fibroblast growth factor 12 isoform 2; fibroblast growth factor 12 isoform 3; fibroblast growth factor 12 isoform 18; fibroblast growth factor 13 isoform 18; fibroblast growth factor 13 isoform 18; fibroblast growth factor 13 isoform 18 1123524.1 Unknown (protein for MGC;26659) 1136401.1 fibroblast growth factor 13 isoform 1B 1136401.1 fibroblast growth factor 13 isoform 1B				Q92912	FGFC_HUMAN Fibroblast growth factor-12 (FGF-12) (Fibroblast growth factor homologous factor 1) (FHF-1) (Myocyte-activating factor)	273	2e-73
194239.1 fibroblast growth factor 13, isoform 1A; fibroblast growth factor homologous factor 2 246 1913 FGFD HUMAN Fibroblast growth factor-13 (FGF-13) (Fibroblast growth factor 2) (FHF-2) 1919 FGFD HUMAN Fibroblast growth factor 2 246 1919 Homologous factor 2) (FHF-2) 1919 FGFD HUMAN Fibroblast growth factor homologous factor 2 246 1919 FGFD HUMAN Fibroblast growth factor 13 isoform 1A 1919 FGFD HUMAN Fibroblast growth factor 13 isoform 2 246 1919 FGFD HUMAN Fibroblast growth factor 12 isoform 2; fibroblast growth factor 12 isoform 18; fibroblast growth factor 1 human 1919 FGF-12b 1910			1	AAB18913.1	fibroblast growth factor homologous factor 1	273	2e-73
PGFD_HUMAN Fibroblast growth factor 13, isoform 1A; fibroblast growth factor 12, 246 FGFD_HUMAN Fibroblast growth factor 13 (FGF-13) (Fibroblast growth factor 13, 1246 Inmologous factor 2) (FHF-2) S18914.1 fibroblast growth factor homologous factor 2 S18914.1 fibroblast growth factor homologous factor 2 S16400.1 fibroblast growth factor 13 isoform 1A S246 S241 S251 FGF-12b FGF-12b FGF-12b FGF-12b FGF-12b S251 S251 S252 S256 S253 S252 S253 S253 S254 S256 S256				CAA94239.1	fibroblast growth factor 11	261	5e-70
FGFD_HUMAN Fibroblast growth factor-13 (FGF-13) (Fibroblast growth factor 2) (FHF-2) 18914.1 fibroblast growth factor homologous factor 2 112347.1 fibroblast growth factor 13 isoform 1A 112347.1 AAH12347 Unknown (protein for MGC:20109) 134340.1 fibroblast growth factor 13 13504104.3 fibroblast growth factor 12 isoform 2; fibroblast growth factor 12 isoform 13; fibroblast growth factor 12 isoform 18; fibroblast growth factor 2 137866.1 fibroblast growth factor 13 isoform 18; fibroblast growth factor 13 isoform 18 1378668.1 fibroblast growth factor 13 isoform 18 138786.1 fibroblast growth factor 13 isoform 18 138786.2 fibroblast growth factor 13 isoform 18 138786.3 fibroblast growth factor 13 isoform 18 138786.3 fibroblast growth factor 13 isoform 18 138786.3 fibroblast growth factor 13 isoform 18 1387868.1 fibroblast growth factor 13 isoform 18		* i .		NP_004105.1	fibroblast growth factor 13, isoform 1A; fibroblast growth factor homologous factor 2	246	
\$18914.1fibroblast growth factor homologous factor 2246\$16400.1fibroblast growth factor 13 isoform 1A246\$112347.1AAH12347 Unknown (protein for MGC:20109)246\$134340.1fibroblast growth factor 13223\$1504104.3fibroblast growth factor 12 isoform 2; fibroblast growth factor 12B; fibroblast growth factor 12B fibroblast growth factor 12B fibroblast growth factor - human221\$184fibroblast growth factor - human221\$18786.3fibroblast growth factor I3 isoform 1B; fibroblast growth factor 13 isoform 1B; fibroblast growth factor 13 isoform 1B213				Q92913	FGFD_HUMAN Fibroblast growth factor-13 (FGF-13) (Fibroblast growth factor homologous factor 2) (FHF-2)	246	2e-65
112347.1AAH12347 Unknown (protein for MGC:20109)246112347.1AAH12347 Unknown (protein for MGC:20109)246134340.1fibroblast growth factor 13223134340.1fibroblast growth factor 12 isoform 2; fibroblast growth factor 12B; fibroblast growth factor 1223184fibroblast growth factor - human22118786.3fibroblast growth factor - human22122524.1Unknown (protein for MGC:26659)219378668.1fibroblast growth factor 13 isoform 1B; fibroblast growth factor 13 isoform 1B213					fibroblast growth factor homologous factor 2	246	2e-65
112347.1AAH12347 Unknown (protein for MGC:20109)246134340.1fibroblast growth factor 13246134340.1fibroblast growth factor 12 isoform 2; fibroblast growth factor 12B; fibroblast growth factor 1223myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor - human221184fibroblast growth factor - human221122524.1Unknown (protein for MGC:26659)219378668.1fibroblast growth factor 13 isoform 1B; fibroblast growth factor 13 isoform 1B213					fibroblast growth factor 13 isoform 1A	246	2e-65
134340.1 fibroblast growth factor 13 soform 2; fibroblast growth factor homologous factor 1; 223 myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor 1; FGF-12b fibroblast growth factor human fibroblast growth factor 3 soform 1B; fibroblast growth factor 13 isoform 1B; fibroblast growth factor 13 isoform 1B fibroblast growth factor 13 isoform 18 fibroblast growth factor 13 isoform 18 fibroblast growth factor 13 isoform 18 fibroblast growth factor			· .	H12347.1	AAH12347 Unknown (protein for MGC:20109)	246	2e-65
myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor 1; RGF-12b 184 fibroblast growth factor - human 18786.3 fibroblast growth factor 18.18786.3 fibroblast growth factor 18.2524.1 Unknown (protein for MGC:26659) 27.1 27.2524.1 fibroblast growth factor 13 isoform 1B; fibroblast growth factor 13 isoform 1B 27.3 27.1 27.1 27.1 27.1 27.1 27.1 27.1 27.1				H34340.1	fibroblast growth factor 13	246	2e-65
184 fibroblast growth factor - human 18786.3 fibroblast growth factor 122524.1 Unknown (protein for MGC:26659) 271 271 271 271 271 271 271 27				004104.3	fibroblast growth factor 12 isoform 2; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	223	2e-58
122524.1 Unknown (protein for MGC:26659) 279 279 279 279 279 279 279 279 279 279	.:			JG0184	fibroblast growth factor - human	221	7e-58
122524.1 Unknown (protein for MGC:26659) 378668.1 fibroblast growth factor 13 isoform 1B; fibroblast growth factor homologous factor 2 213 216401.1 fibroblast growth factor 13 isoform 1B				B18786.3	fibroblast growth factor	221	7e-58
378668.1 fibroblast growth factor 13 isoform 1B; fibroblast growth factor homologous factor 2 213		<i>i</i>	: ::	122524.1	Unknown (protein for MGC:26659)	219	2e-57
D16401.1 fibroblast growth factor 13 isoform 1B				378668.1	fibroblast growth factor 13 isoform 1B; fibroblast growth factor homologous factor 2	213	1e-55
				D16401.1	fibroblast growth factor 13 isoform 1B	213	1e-55

206 e-107 e-107 e-106 e-106 e-105 e-105 e-105 e-105 5e-78 6e-97 5e-78| 5e-78 2e-75 2e-75 7e-62 1e-55 1e-551e-551e-55 386 386 386 379 386 382 379 289 289 382 379 352 289 236 215 281 281 ficolin 2 isoform b precursor; ficolin (collagen/fibrinogen domain-containing lectin) 2 (hucolin); ficolin (collagen/fibrinogen domain-containing lectin) 2; hucolin ficolin 2 isoform a precursor; ficolin (collagen/fibrinogen domain-containing lectin) 2 FCN3_HUMAN Ficolin 3 precursor (Collagen/fibrinogen domain-containing protein 3) (Collagen/fibrinogen domain-containing lectin 3 p35) (Hakata antigen) FCN1_HUMAN Ficolin 1 precursor (Collagen/fibrinogen domain-containing protein FCN2_HUMAN Ficolin 2 precursor (Collagen/fibrinogen domain-containing protein ficolin 3 precursor; ficolin (collagen/fibrinogen domain-containing) 3 (Hakata Similar to ficolin (collagen/fibrinogen domain-containing) 3 (Hakata antigen) 2) (Ficolin-B) (Ficolin B) (Serum lectin p35) (EBP-37) (Hucolin) (L-Ficolin) (hucolin); ficolin (collagen/fibrinogen domain-containing lectin) 2; hucolin microfibrillar-associated protein 4; microfibril-associated glycoprotein 4 001994.2 ficolin 1 precursor; ficolin (collagen/fibrinogen domain-containing) 1 MFA4 HUMAN Microfibril-associated glycoprotein 4 precursor ficolin (collagen/fibrinogen domain-containing) 1 similar to Microfibril-associated glycoprotein 4 1) (Ficolin-A) (Ficolin A) (M-Ficolin) microfibril-associated glycoprotein 4 AAH32953.1 Unknown (protein for MGC:33476) unnamed protein product ficolin-1 precursor serum lectin P35 Hakata antigen BAA09636.1 lectin P35 antigen) ficolin ficolin BAA08352.1 NP_056652.1 NP_003656.1 XP 045044.2 NP 004099.1 AAH20635.1 AAH20731.1 NP 002395.1 AAB50706.1 BAA32277.1 AAB00968.1 BAA12120.1 BAC11429.1 O00602 015485 075636 S61517 P55083 æ U:(C-IR) 2.21 U:(C-D) 2.45 Mm.10510 NP 032021.1 : :: NM 007995

	e-110	e-110	e-110	0		2e-56	Ze-56	50.55	3e-54	30 54	3e-54	36-54	. 3e-54	3e-54	1e-52	1e-52	1e-52	1e-52	1e-52	1e-52
	398	397	397	9/_	922	218	218	213	211	2111	211	211	211	211	206	206	206	206	206	206
	I hypothetical protein	1 hypothetical protein FLJ32702	unnamed protein product	similar to amiloride-sensitive sodium channel	amiloride-sensitive sodium channel	sodium channel 2	2 amiloride-sensitive cation channel 2, neuronal isoform b; hBNaC2; Cation channel, amiloride-sensitive, neuronal, 2		testis amiloride-sensitive cation channel 3, isoform b; testis sodium channel 1; proton-gated cation channel subunit; modulatory subunit of ASIC2a				testis amiloride-sensitive cation channel 3, isoform c; testis sodium channel 1; proton-gated cation channel subunit; modulatory subunit of ASIC2a	AF195024_1 acid sensing ion channel 3 splice variant b	neuronal amiloride-sensitive cation channel 1; degenerin	BNA1_HUMAN Amiloride-sensitive brain sodium channel BNaC1 (Amiloride-sensitive cation channel neuronal 1) (BNC1) (Degenerin channel MDEG)	degenerin channel MDEG	sodium channel 1	sodium channel 1	Na channel
	XP_063839.1	NP 689550.1	BAB71401.1	XP_032835.1	CAB85607.1	AAB48981.1	NP_001086.2	AAC62935.1	NP_064717.1	AAF19818.1	NP_004760.1	ÅAC64188.1	NP_064718.1	AAF19817.1	NP_001085.2	Q16515	AAC50498.1	AAB49182.1	AAC50432.1	2211325A
U:(C-IR) 2.2 U:(C-D) 2.58 11:(78, p)	2.72			U:(C-R) 2.19		,				÷										
	Mm.59283). 	Mm.8883 9				ţ *		:							:	. ,		
AK006553	BAB24650.1			NM_021370 NP_067345.1							A :			·						

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1	26-52	5e-52 e-118		e-118	e-118	e-110 2e-69		2e-69	28-60	28-69	36-55	3	36.03	20 02	36-93	58-87	2e-79	26-79	2e-79	2e-79
500	203	424		424	424	399		259	250	250	212		340	340	340	310	293	293	293	293
testis sodium channel 1		1 claudin 18	CIDI HIMAN Clandin 18		•			RET7_HUMAN Retinol-binding protein IV, cellular (CRBP-IV) (Retinoid binding protein 7)	٠.,	putative cellular retinol-binding protein CRBP IV			1 cell death-inducing DFFA-like effector a	CIDA_HUMAN Cell death activator CIDE-A (Cell death-inducing DFFA-like effector A)				hypothetical protein	AAH00705 Unknown (protein for MGC:861)	AAH07495 hypothetical protein MGC861
JE0091	BAA25897.1	NP_057453.1	P56856	AAF26448 1	AAL15637.1	NP_443192.1		Q96R05	AAK85409.1	AAN61071.1	AAH33883.1		NP_001270.1	060543	AAC34987.1	AAH31896.1	NP_076958.1	CAB77147.1	AAH00705.1	AAH07495.1
		U:(C-IR) 2.17 U:(C-D)	2.12			U:(C-IR)	U:(C-D) 2.04	-		•		11-(C-IR)	2.16			4.4	U:(C-IR) 2.16		; ;	
		U:(C-IR) 2.17 Mm.3509 U:(C-D)	0		,		Mm.4602 3	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \				, i	Mm.449				Mm.2359 6			
			NP 062789.1				NM_022020 NP_071303.1					NM_007702	NP 031728.1				NM_025639 NP_079915.1			

ATA COSCOLA	0.00	-				
NP 080110.1	1Mm.8079 8	U:(C-IR) 2.16	NP_003882.1	protein $Z_{\rm s}$, vitamin K-dependent plasma glycoprotein	260	e-159
			P22891	PRTZ_HUMAN Vitamin K-dependent protein Z precursor	560	P-150
			AAA36500.1	m protein Z	260	727
			BAA85763.1	protein Z.	260	6-139
			AAL27631.1	AF440358 1 protein Z, vitamin K-dependent plasma glycoprofein	200	e-139
,			KXHUZ	plasma protein Z precursor	550	0-135
			AAA36501.1	protein Z	550	0CI-0
			BAA85764.1	protein Z spliced variant	550	P-156
,		; .	AAA36499.1	protein Z	454	e-127
			AAA51984.1	coagulation factor X precursor	214	76-55
			1205236A	coagulation factor X	214	79-55
			AAA52490.1	factor X prepeptide	213	16-54
	.)		NP_000495.1	coagulation factor X precursor; Prothrombinase	213	10 54
			P00742	FA10 HUMAN Coagulation factor X precursor (Stuart factor)	212	10.54
	•		EXHU	coagulation factor Xa (EC 3.4.21.6) precursor	213	10-54
ţ		, i	AAA52421.1	coagulation factor X	213	10-54
			AAA52764.1	coagulation factor X	213	16-54
			AAM19347.1	AF503510_1 coagulation factor X	213	1e-54
			21954.1	F9 (coagulation factor IX (plasma thromboplastic component, Christmas disease, haemophilia B))	201	6e-51
			NP_000124.1	coagulation factor IX; Coagulation factor IX (plasma thromboplastic component); Factor 9; Factor IX; Christmas factor	201	6e-51
	•		AAA52023.i	coagulation factor IX precursor	201	6e-51
		·	AÅA52763.1	factor IX (Christmas factor) precursor	201	6e-51
			AAM96188.1	coagulation factor IX (plasma thromboplastic component, Christmas disease, hemophilia B)	201	6e-51
:		•	P00740	FA9_HUMAN Coagulation factor IX precursor (Christmas factor)	201	6e-51
			KFHU	coagulation factor IXa (EC 3.4.21.22) precursor	201	6e-51
						- 4 3 3 3

		,	AAB59620.1	factor IX		
		\ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	AAA56822.1	factor IX	201	6e-51
			A A A 08726 1	factor IV	701	
1116160		1	1.02/0/22/27	ALI TAYOU TAY	199	3e-50
AAC52197.1	Mm.2212	U:(C-1K) 2.16	DAHUA1	procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 1	1001	0
	,		AAA59069.1	alpha-subunit of prolyl 4-hydroxylase	190	·
			NP_000908.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I; procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polymentide 1	991	0
			AAA36534.1	prolyl 4-hydroxylase alpha subunit (EC 1.14.11.2)	901	Ċ
		:	P13674	P4H1_HUMAN Prolyl 4-hydroxylase alpha-1 subunit precursor (4-PH alpha-1) (Procollagen-proline,2-oxoglutarate-4-dioxygenase alpha-1 subunit)	982	
			DAHUA2	procollagen-proline dioxygenase (BC 1.14.11.2) alpha chain precursor, splice form 2	982	210
			AAA59068.1	alpha-subunit of prolyl 4-hydroxylase	982	0
			AAH34998.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I	985	0
			AAA36535.1	prolyl 4-hydroxylase alpha subunit (EC 1.14.11.2)	971	0
		***	NP_004190.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II, prolyl 4-hydroxylase, alpha polypeptide, type 2; prolyl-4-hydroxylase, alpha polypeptide, type II	629	0
			015460	P4H2_HUMAN Prolyl 4-hydroxylase alpha-2 subunit precursor (4-PH alpha-2) (Procollagen-proline, 2-oxoglutarate-4-dioxygenase alpha-2 subunit)	629	0
			AAB71339.1	prolyl 4-hydroxylase alpha (II) subunit	6/9	0
	:		CAC85689.1	Prolyl 4-hydroxylase alpha IIb subunit	679	0
		·	CAC85688.1	Prolyl 4-hydroxylase alpha IIa subunit	658	0
			AAH35813.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II	658	0
		U:(C-IR)	NP_002603.1	pyruvate dehydrogenase kinase, isoenzyme 4	764	0
NM_013743 NP_038771.1	Mm.1028 3	U:(C-D) 2.04			·	

				The second secon		
	•	,	Q16654	PDK4_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 4, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 2)	764	0
1:	,•-	,	AAC50669.1	pyruvate dehydrogenase kinase isoform 4	764	
,			AAC50670.1	pyruvate dehydrogenase kinase isoform 4	107	
			AAB67048.1	DVIIIVATE delividrogenage brinsse isoform /	104	٥
			A A EZA0220 1	Francis and an explanation and an explanation of the explanation of th	/64	0
			AAII40239,1	pyruvaie denydrogenase kinase, isoenzyme 4	764	-0
			NP_002601.1	pyruvate dehydrogenase kinase, isoenzyme 1	562	e-159
			Q15118	PDK1_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 1, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 1)	562	e-159
			I55465	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 1	562	P-150
		· · ·	AAC42009.1	pyruvate dehydrogenase kinase	562	
	:		AAH39158.1	Similar to pyruvatė dehydrogenase kinase, isoenzyme 1	562	6-159
	# -		2203383A	pyruvate dehydrogenase kinase:ISOTYPE=1	562	e-159
		٠,	NP_002602.2	pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
			Q15119 	PDK2_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 2, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 2)	556	e-157
,			AAH05811.1	AAH05811 pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
4.00			AAH40478.1	pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
		****	170159	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 2	554	e-157
	1		AAC42010.1	pyruvate dehydrogenase kinase	554	e-157
			2203383B	pyruvate dehydrogenase kinase:ISOTYPE=2	554	e-157
			NP_005382.1	pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
			Q15120	PDK3_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 3, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 3)	527	e-149
			170160	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 3	527	e-149
			AAC42011.1	pyruvate dehydrogenase kinase	527	e-149
			AAH15948.1	AAH15948 pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
			2203383C	pyruyate dehydrogenase kinase:ISOTYPE=3	703	P-1/10

NM_025806 NP_080082.1	Mm.3311	U:(C-IR) 2.15	NP_079105.1	hypothetical protein FLJ22662	870	0
			BAB15442.1	unnamed protein product	870	0
			AAH00909.2	AAH00909 hypothetical protein FLJ22662	307	P-11
		l.	XP_113725.2	similar to RIKEN cDNA 1300012G16	27.1	
	•		AAH30618.1	similar to RIKEN cDNA 1300012G16	771	
NM 008030		U:(C-IR) 2.14			7 7	71-07
_ NP_032056.1	Mm.2900	U:(C-D) 2.22	P31513	FMO3_HUMAN Dimethylaniline monooxygenase [N-oxide forming] 3 (Hepatic flavin-containing monooxygenase 3) (FMO 3) (Dimethylaniline oxidase 3) (FMO II)	847	
		t	AAC51932.1	flavin containing monooxygenase 3	847	
	` ` `			dJ127D3.1 (Hepatic Flavin-containing Monooxygenase 3 (Dimethylaniline Monooxygenase (N-Oxide forming) 3, EC1.14.13.8, Dimethylaniline Oxidase 3.		
-	·		CAA15908.1	FMO II, FMO 3))	847	0
		,	AAH32016.1	flavin containing monooxygenase 3	847	0
			NP_008825.2	flavin containing monooxygenase 3; Flavin-containing monooxygenase-3	846	C
			S51130	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8) 3	846	0
			CAA87632.1	flavin-containing monooxygenase 3 (FMO3)	846	0
			A38228	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8), hepatic 2	795	0
			AAA86284.1	flavoprotein	795	0
•	-	·	CAA15909.1	dJ127D3.2 (Flavin-containing Monooxygenase family protein)	770	0
		·		FMO2_HUMAN Dimethylaniline monooxygenase [N-oxide forming] 2 (Pulmonary flavin-containing monooxygenase 2) (FMO 2) (Dimethylaniling cridges 2) (FMO 2)		
-	•	1.	Q99518	1B1)	610	e-174
			NP_002012.1	flavin containing monooxygenase 1; Flavin-containing monooxygenase 1 (fetal liver)	580	<u> </u>
				FMO1_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE		
			Q01740	FORMING 1 (FELAL HEPALIC FLAVIN-CONTAINING MONOOXYGENASE 1) (FMO 1) (DIMETHYLANILINE OXIDASE 1)	580	e-165
,			A40876	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8), hepatic 1	580	e-165
			AAA52457.1	flavin-containing monooxygenase	580	e-165
					. 500	

	:	1	NP_001451.1	flavin containing monooxygenase 2; Flavin-containing monooxygenase 2 (adult liver)	195	P-150
			CAA70462.1	flavin-containing monooxygenase 2	\perp	P-150
			CAA15910.1	dJ127D3.3 (Flavin-containing Monooxygenase 2)	195	0 150
			AAH05894.1	flavin containing monooxygenase 2	561	e-150
			9C50Fd	FMO5_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE FORMING] 5 (HEPATIC FLAVIN-CONTAINING MONOOXYGENASE 5) (FMO		
			S71618	dimethylanline monoxygenase (N. oxide forming) (DC 1.14.12.0) mx roc	546	e-155
			AAA67849.1	flavin-containing monooxygenase 5	240	e-155
			NP_001452.1	flavin containing monooxygenase 5	545	6-155
		, ,	S51131	flavin-containing monooxygenase 5 (FMO5)	545	e-155
	* .	,	CAA87633.1	flavin-containing monooxygenase 5 (FMO5)	545	P-155
NM_011012_ NP_035142.1	Mm.2991	U:(C-IR) 2.14	NP_000904.1	opiate receptor-like 1; opioid receptor-like 1; kappa3-related opioid receptor	573	e-163
			P41146	OPRX_HUMAN Nociceptin receptor (Orphanin FQ receptor) (Kappa-type 3 opioid receptor) (KOR-3)	573	e-163
			S43087	orphan opioid receptor ORL1	573	e-163
	3	· :	CAA54386.1	ORL1	573	e-163
			AAA84913.1	orphan opioid receptor	573	e-163
		3	AAK11714.1	AF348323_1 nociceptin receptor	573	e-163
			AAH38433.1	opiate receptor-like 1	573	e-163
		٠	AAL54890.1	AF126470_1 KOR-3D	558	e-159
			AAA96251.1	opioid receptor-like protein	509	e-144
			2201468A	opioid orphan receptor	509	e-144
\ \-			CAC17003.1	dJ1022E24.1 (opiate receptor-like protein 1 (OPRL1))	445	e-125
	:	.:	CAC15482.1	dJ366F13.1 (opioid receptor mu 1)	296	4e-80
		٠	P35372	OPRM_HUMAN Mu-type opioid receptor (MOR-1)	296	4e-80
			156553	mu opiate receptor	296	4e-80
		;	AAA73958.1	opioid receptor	296	4e-80

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L	46-80		\perp				1e-76		e-76	e-153			<u> </u>	<u> </u>	3e-70		3e-60					
200	2062	206	202	567	293	285	285	285	239	530	530	267	7.92	264	264	231	231	758	758	758	758	758
mu opioid receptor	1 opioid receptor, mu 1	Mu opiate receptor	opioid receptor mu variant MOR1A					drata optate receptor		NER2_HUMAN Sialidase 2 (Cytosolic sialidase) (N-acetyl-alpha-neuraminidase 2)		sialidase 3; neuraminidase 3; ganglioside sialidase; N-acetyl-alpha-neuraminidase 3	Nuraminidase	NER3_HUMAN Sialidase 3 (Membrane sialidase) (Ganglioside sialidase) (N-acetyl-alpha-neuraminidase 3)	ganglioside sialidase	sialidase	sialidase	similar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	NAL4_HUMAN NACHT-, LRR- and PYD-containing protein 4 (PAAD and NACHT-containing protein 2) (PYRIN-containing APAF1-like protein 4) (Ribonuclease inhibitor 2)	AF442488_1 NALP4	PAAD and NACHT-containing protein 2
2108340A	NP_000905.1	AAA20580.1	S65693	AAB60354.1	AAN87342.1	P41143	1 70 8340 A A	CAA15671.1	NP_005374.1	Q9Y3R4	CAB41449.1	NP 006647.2	CAB96131.1	Q9UQ49	BAA82611.1	CAC81904.1	NP 542779.2	XP_085972.4	NP_604393.1	O96MN2	AAL35293.1	AAL68396.1
	·					Ţ			U:(C-IR) 2.14			:			' '1 '			U:(C-IR) 2.14			,	
	·								Mm,4567 0					1.				Mm.8479 2		1		·.
					- }-				NM_015750 NP_056565.1	i								NM_031389 NP_113566.1				

			AAL87104.1	AF479747_1 PYRIN-containing APAF1-like protein 4	758	0
	.1		BAB71254.1	unnamed protein product	758	
		į	AAL88672.1	AF482706_1 ribonuclease inhibitor 2	740	
	1	:	XP_062261.4	similar to PYRIN-containing APAF1-like Protein 7	\$ \\ \frac{1}{2}	0 120
			NP_659444.1		427	e-110
		ij	P59045	PYA6_HUMAN PYRIN-containing APAF1-like protein 6	427	e-119
		:	AAM14632.1	PYRIN-containing APAF1-like protein 6	477	e-110
•		÷	AAH34730.1	PYRIN-containing APAF1-like protein 6	427	-110
	-		AAH16443.1	AAH16443 Unknown (protein for IMAGE:3448931)	301	0 100
			AAL78632.1	AF468522_1 NALP3 long isoform	370	100
1			NP 004886.2	Cold autoinflammatory syndrome 1. ohromosome 1 onen reading fame 7.	040	+01-0
			I	angiotensin/vasopressin receptor AII/AVP-like; cryopyrin; PYRIN-containing APAF1-like protein 1	8/c	-9 104-104
			Q96P20	CIS1_HUMAN Cold autoinflammatory syndrome 1 protein (Cryonyrin) (NACHT.	378	104
				LRR-and PYD-containing protein 3) (PYRIN-containing APAF1-like protein 1) (Angiotensin/vasonressin recentor AII/AVD-147-a)	2	† 0
			AAT.33908.1	AF410477 1 cryonymin	0.00	
			, 10,0,1		2/8	e-104
,			AAL12497.1	cryopynin	378	e-104
;			AAL65136.1	AF420469_1 PYRIN-containing APAF1-like protein 1	378	e-104
	,,		XP_064988.5	sumilar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	367	e-101
NM_025621 NP_079897.1	Mm.1442 59	U:(C-IR) 2.11	XP_088993.1	similar to RIKEN cDNA 2310050C09	229	5e-60
n .		,				
NM_011377 NP_035507.1	Mm.4775	U:(C-IR) 2.09	NP_005060.1	single-minded (Drosophila) homolog 2 long isoform; human transcription factor SIM2, homolog of the Drosophila single-minded gene SIM1	939	0
		:	Q14190	SIM2_HUMAN Single-minded homolog 2	939	0
	1		AAB62396.1	transcription factor SIM2 long form	939	0
			BAA89433.1	single-minded 2 protein	939	0

51			NP_033664.1	single-minded (Drosophila) homolog 2 short isoform; human transcription factor SIM2, homolog of the Drosophila single-minded oene SIM1	849	0
			AAB62397.1	transcription factor SIM2 short form	070	
			CAA05055.1	human SIM2	720	
		1	NP_005059.2	single-minded (Drosophila) homolog 1: Single-minded drosonhila homolog of 1	671	
			P81133	SIM1_HUMAN Single-minded homolog 1	450	0
		1	AAB62395.1	hSIM1	670	G-190
1			A58520	Single-minded gene 2 profein	670	e-180
			BAA12919.1	Sim	462	e-129
			NP 071406.1	basic-helix-loop-helix-PAS protein	401	e-129
				AF164438 1 hasic-helix-loon-haliv DAS meeting	C67	3e-79
			BAB21221.1	NPAS3 (MOP6)	295	3e-79
					295	Se-79
11001011			BAC53756.1	NPAS3	295	.5e-79
AF319951 AAL37178.1	Mm.35253	U:(C-IR) 2.08	AAM73657.1	solute carrier family 12 member 8	1011	<
			AAK94307.1	solute carrier family 12 member 8	7,66	
			AAH20506.1	hypothetical protein FLJ23188	370	P-102
• • • • • • • • • • • • • • • • • • •	\		NP 078904.1	solute carrier family 12 (potassium/chloride transporters), member 8; solute carrier family 12 (sodium/potassium/chloride transporters) member 8	2 6	701
			BAB15571.1	unnamed protein product	369	e-101
		:	NP_001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters)	270	2 × 0
		-	P55011	S122_HUMAN Solute carrier family 12 member 2 (Burnetanide-sensitive	230	20.50
			A57187	bumetanide-sensitive Na-K-Cl cotransporter	2300	26-33
			AAC50561.1	bumetanide-sensitive Na-K-Cl cottansporter	229	2e-50
			AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride	229	2e-59
			NP_000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12	223	1e-57
1.			Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitive	. 223	1e-57
			AAB07364.1	bumetanide-sensitive Na-K-2Cl cotransporter	223	16-57

		,	P55017	S123_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride	201	12 0
		1		solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier	707	10-04
				family 12 (sodium/potassium/chloride transporters),	201	4e-51
			AAC50355.1	thiazide-sensitive Na-Cl	201	4e-51
		:	G01202	NaCl electroneutral Thiazide-sensitive cotransporter	201	5e-51
			CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	201	5e-51
NM_008074		,				
NP 0321001	Mm 1345	U.(C-IR)	NP 150002 1	1 (1 ft f) E		············
T-001770 TLT		4. 00	1.220021_1vi	gamma-ammobutyric acid (GABA) A receptor, gamma 3	841	0
) -			AAB39369.1	GABAA receptor gamma 3 subunit	841	0
	•		099928	GAC3_HUMAN Gamma-aminobutyric-acid receptor gamma-3 subunit precursor (GABA(A) receptor)	838	21
			AAF99698.1	GABAA receptor gamma 3 subunit	838	
		,	AAF63215.1	GABAA receptor gamma 3 subunit	928	
•			AAD50273.1	gamma-aminobutyric acid A receptor gamma 2	288	p 167
· 1			NP_000807.1	gamma-aminobutyric acid A receptor, gamma 2 precursor	584	e-166
	i	!		GAC2_HUMAN Gamma-aminobutyric-acid receptor gamma-2 subunit precursor		
			P18507	(GABA(A) receptor)	584	e-166
	,		S03905	gamma-aminobutyric acid/benzodiazepine receptor gamma-2 chain precursor	584	e-166
			CAA33437.1	GABA-A receptor gamma 2 subunit	584	e-166
	1		1506443A	GABAa receptor gamma2	584	e-166
			AAH31087.1	similar to GAMMA-AMINOBUTYRIC-ACID RECEPTOR GAMMA-1 SUBUNIT PRECURSOR (GABA(A) RECEPTOR)	576	e-164
		,		similar to Gamma-aminobutyric-acid receptor gamma-1 subunit precursor (GABA(A)		
			094080.1	receptor) [Homo sapiens]	276	e-164
)	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	NP_004952.1	gamma-aminobutyric acid (GABA) A receptor, epsilon, isoform 1 precursor	378	e-104
		j.	AAB49284.1	GABA-A receptor epsilon subunit	378	e-104
			P78334	GABEA(A) receptor)	378	e-104

			CAA70904.1	GABA receptor epsilon subunit	378	P-104
			AAB94645.1	GABA-A receptor epsilon subunit	378	
,) ;		CAA70903.1	GABRE	374	
NM_010899 NP_035029.1	Mm.1168 02	U:(C-IR) 2.08	Q13469	NFC2_HUMAN Nuclear factor of activated T-cells, cytoplasmic 2 (T cell transcription factor NFAT1) (NFAT pre-existing subunit)(NF-ATp)	1522	
	i.		AAC50887.1	transcription factor NFAT1 isoform C	1522	C
		; ;	NP_036472.1	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2; nuclear factor of activated T-cells, cytoplasmic 2	1487	
		· .	G02326	transcription factor NFAT1 isoform B - human	1487	0
			AAC50886.1	transcription factor NFAT1 isoform B	1487	
			CAC00528.1	d1994O24.1 (nuclear factor of activated T-cells, cytoplasmic 2 (isoforms B and C))	835	
			CAB54871.1	dJ1009H6.1.2 (nuclear factor of activated T-cells, cytoplasmic 2, isoform C)	649	
	1		CAC00529.1	dJ1009H6.1.1 (nuclear factor of activated T-cells, cytoplasmic 2, isoform B)	615	e-17
			1A02	N Chain N, Structure Of The Dna Binding Domains Of Nfat, Fos And Jun Bound To Dna	267	
N 1			AAD00451.1	transcription factor	551	e-156
			095644	NFC1_HUMAN Nuclear factor of activated T-cells, cytoplasmic 1 (NFAT transcription complex cytosolic component) (NF-ATc1) (NF-ATc)	550	e-156
		*	AAC50869.1	nuclear factor of activated T cells	523	e-148
	·÷	,	NP_006153.2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1; nuclear factor of activated T-cells, cytoplasmic 1	521	e-147
	, .		AAD00450.1	transcription factor	521	e-147
	. :'	U:(C-IR)	NP_037504.1	cysteine knot superfamily 1, BMP antagonist 1; gremlin	311	2e-84
NM_011824 NP_035954.1	Mm.3046 5	U:(C-D) 2.59				
			AAC39725.1	gremlin	311	2e-84
	:		BAA84462.1	gremlin homologue	311	2e-84
			AAF06677.1	gremlin	311	2e-84
			AAG23891.1	AF154054 1 DRM	. 311	2e-84

		,,,	,00.	2398	,								219	•							. 1, C		05/	000		
. 3e-67	8e-67					e-142	e-142	e-142	e-142	e-142	7e-75	4e-56	4e-56	4e-56	2e-55	2e-55	2e-55	2e-55	,	e-149	e-149	e-147	e-147	8e-50	8e-50	02.50
254	253					505	505	505	505	504	280	218	218	218	216	216	216	216		527	527	521	521	1961	196	106
uniamed protein product	unnamed protein product				2 similar to Homeobox protein Hox-C13 (Hox-3G)	2 homeo box C13; homeobox protein Hox-C13; homeo box 3G	HXCD_HUMAN Homeobox protein Hox-C13 (Hox-3G	HOXC13	homeo box C13	homeoprotein C13	unnamed protein product	HXAD_HUMAN Homeobox protein Hox-A13	transcription factor HOXA13	homeobox protein A13; homeobox protein HOXA13; homeo box 1J; transcription factor HOXA13	homeo box D13; homeo box 4I; homeobox protein Hox-D13	HXDD_HUMAN Homeobox protein Hox-D13 (Hox-4I)	HOXD13	homeobox transcription factor		similar to G protein-coupled receptor 65; T-cell death-associated gene 8	similar to G protein-coupled receptor	G protein-coupled receptor 65; T-cell death-associated gene 8	T cell-death associated protein	G protein-coupled receptor 6C.1	G protein-coupled receptor	G protein-compled recentor
DAC04020.1	BAC04643.1				XP_006804.2	NP 059106.2	P31276	AAF73439.1	AAH02754.1	AAF67760.1	BAB14786.1	P31271	AAC50993.1	NP_000513.2	NP_000514.1	P35453	AAC51635.1	BAA95352.1		XP 007392.1	AAH35633.1	NP_003599.1	AAC31794.1	S68207	AAA79061.1	2124311B
: :			:	U:(C-IR)	2.07											-			U.(C-IR)	2.07			ī	/:		
				Mm.20706	2						. (,					1	1		Mm.2840		-				
					AAL09298.1						- 1							,	NM_008152	NP_032178.1						

			NP 005273.1	G protein-coupled receptor 4	196	80.50
1		·	XP_009140.1	similar to Probable G protein-coupled receptor GPR4 (GPR19)	5 5	8 50
. ,			P46093	GPR4_HUMAN Probable G protein-coupled receptor GPR4 (GPR 19)	106	80.50
	7.7 37		A57641	G protein-coupled receptor 4	106	00-20
	-		AAA98457.1	G protein-coupled receptor	100	00-00 .
, 3			I53033	G protein-coupled receptor	1 2	8P-50
;			AAA63180.1	G protein-coupled receptor	196	8 50
NM_008324 NP_032350.1	Mm.392	U:(C-R) 2.07	NP 002155.1	indoleamine-pyrrole 2,3 dioxygenase; Indoleamine 2,3-dioxygenase; indole 2,3-dioxygenase	9	141
î ;	;			1230_HUMAN Indoleamine 2,3-dioxygenase (IDO) (Indoleamine-pyrrole 2,3-dioxygenase)	400	27
			PC1161	indoleamine-pyrrole 2,3-dioxygenase (EC 1.13.11.42)	499	20 141
. 1			CAA35663.1	indoleamine 2,3-dioxygenase	499	e-141
			AAA36081.1	indoleamine 2,3-dioxygenase (IDO) (EC 1.13.11.17)	499	e-141
			AAH27882.1	indoleamine-pyrrole 2,3 dioxygenase	. 499	e-141
:			XP_095645.4	similar to indoleamine 2,3-dioxygenase	313	46-85
NM_009827	!					2
NP_033957.1	Mm.3521	U:(C-IR) 2.07	NP_000721.1	000721.1 cholecystokinin A receptor	. 693	
			P32238	CCKR_HUMAN Cholecystokinin type A receptor (CCK-A receptor) (CCK-AR)	693	0
		, 1 0.	JN0692	cholecystokinin type A receptor	693	0
		· · · · · · · · · · · · · · · · · · ·	AAA35659.1	cholecystokinin A receptor	693	0
			AAA02819.1	A02819.1 cholecystokinin A receptor	693	0
			AAA91123.1	cholecystokinin type A receptor	693	0
		1 1	BAA90879.1	cholecystokinin type-A receptor	693	0
			2118221A	cholecystokinin A receptor	619	0
	()		P32239	GASR_HUMAN Gastrin/cholecystokinin type B receptor (CCK-B receptor) (CCK-BR)	350	8-96

			A47430	gastrin/cholecystokinin receptor B. short splice form	250	
			AAA35660.1	cholecystokinin receptor	OCC S	
			AAA35657.1	cholecystokinin-B/astrin recentor	350	
			A A C37528 1	gaetrin recentor	320	8e-96
			T 4 4 00 5 C 4 1	Sacrata reversion.	350	8e-96
			DAA02304.1	cholecystokmin receptor	350	96-98
				AAH00740 cholecystokinin B receptor	350	8e-96
		1	AAA91831.1	cholecystokinin B receptor	348	
			AAB30766.2	cholecystokinin B receptor	240	
	:	,	BAA:04759.1	cholecystokinin-B receptor/gastrin receptor	240	
			AAC27510 1	gaetrin) cholamatolymin temin	2,40	46-33
			A A K 38351 1	CCR. P. Inserting research.	345	
			A A N37870	ADMITTO 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	243	16-63
			I		243	1e-63
			NP_000722.2		. 241	5e-63
- 1			AAF67174.1	AF239668_1 CCK-B/gastrin receptor	241	56-63
NM_013920 NP_038948.1	Mm.4198 5	U:(C-IR) 2.07	JC6095	hepatocyte nuclear factor 4 gamma chain	749	0
			2208436B	hepatocyte nuclear factor 4	740	
			NP 004124.2	hepatocyte nuclear factor 4, gamma	730	
			CAA89990.2	hepatocyte nuclear factor 4 gamma (HNF4gamma)	730	2 0
	,	1	Q14541	HN4G_HUMAN Hepatocyte nuclear factor 4-gamma (HNF-4-gamma)	738	
			AAF00110.1	hepatocyte nuclear factor 4 gamma	738	٥
			CAA61133.1	Hepatocyte nuclear factor 4A	482	9 166
		1,1	AAB48082.1	hepatocyte nuclear factor 4-alpha	570	2-165
			NP_000448.2	hepatocyte nuclear factor 4, alpha; transcription factor-14; hepatic nuclear factor 4, alpha	579	e-165
			JC6096	hepatocyte nuclear factor 4 alpha2 chain	570	9 165
No. of the last of			CAA89989.1	hepatocyte nuclear factor 4 alpha (HNF4alpha4)	570	0.165
			2208436A	hepatocyte nuclear factor 4.18OTVPH==11nha	CIC	GIL
			7	freely exercise accountable applies	6/3	e-165

			CAC01303.1	dJ1013A22.1 (hepatocyte nuclear factor 4 alpha)		
			P41235		578	e-165
		•		factor HNF-4) (Transcription factor 14)	<u>,</u>	
			CAA54248.1	hepatocyte nuclear factor 4	576	e-164
				hepatocyte nuclear factor 4, splice form B	575	e-164
			CAA61134,1	Hepatocyte nuclear factor 4B	575	p-164
NM 020028 NP 064412.1	Mm,2325 3	U:(C-IR) 2.07	NP_004711.2	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4; G protein-coupled receptor; lysophosphatidic acid receptor FDG4. 1 D 4 receptor FDG3.	470	c-132
			О9НВМ0	EDG4_HUMAN Lysophosphatidic acid receptor Edg-4 (LPA receptor 2) (TPA-2)	470	130
		:	AAB61528.1	R33799_1	077	0.120
3,			AAF43409.1	AF233092_1 lysophosphatidic acid G protein-coupled recentor 4	7 5	6-132
		T.	AAH25695.1	endothelial differentiation, lysophosphatidic acid G-protein-counled recentor 4	470	22
		7.	AAG28521.1	AF197929_1 lysophosphatidic acid receptor EDG4	468	7 121
			AAC27728.1	G protein-coupled receptor Edg.4	763	6 120
			NP_001392.2		355	0-130
,			476500.1	lysophosphatidic acid receptor EDG2; ventricular zone gene 1: LPA recentor EDG?	255	79-07
			092633	EDG2_HUMAN Lysophosphatidic acid receptor Edg-2 (LPA receptor 1) (LPA-1)	255	2e-67
			CAA70686,1	G protein-coupled receptor Edg-2	255	. 2e-67
		2	AAC00530.1	Edg-2 receptor	255	2e-67
			AAH30615.1	Unknown (protein for MGC:33156)	255	2e-67
			AAH36034.1	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	255	2e-67
			JC5293		255	2e-67
			AAC51139.1	lysophosphatidic acid receptor homolog	255	26-67
			CAA70687.1	G protein-coupled receptor Edg-2	786	Ja.67
			NP_036284.1	endothelial cell differentiation gene 7; calcium-mobilizing lysophosphatidic acid receptor LP-A3; LPA receptor EDG7	225	3e-58
-	, , , ,		Q9UBY5	EDG7_HUMAN Lysophosphatidic acid receptor Edg-7 (LPA receptor 3) (LPA-3)	225	36-58
			AAD56311.1	AF127138 1 lysophosphatidic acid G protein-coupled receptor	225	36-58
	•				777	00-20

			AAF00530.1	AF186380 1 calcium-mobilizing lysophosphatidic acid receptor LP-A3/Ede-7	225	3e-58
			AAF91291.1	G-protein coupled receptor BDG-7	222	2e-57
AK015988		·				
XP_129281.1	U:(C Mm.40665 2.06	U:(C-IR) 2.06	NP_079065.1	hypothetical protein FLJ22529	137	5e-89
			BAB15385.1	unnamed protein product	137	5e-89
	* 3	U:(C-IR)				
NM_009565	17060	2.05			<u>:</u>	
NP_033591.1	Min. 1 / 068 U:(C-D) 4 2.13	0:(ヘーレ) 2.13	AAH12070.1	Similar to kruppel-related zinc finger protein hcKrox	593	e-170
	-		NP_056956.1	kruppel-related zinc finger protein hcKrox	592	
	1,		AAC51847.1	kruppel-related zinc finger protein hcKrox	592	e-170
			XP_113971.1	similar to HIV-1 inducer of short transcripts binding protein	206	9e-53
	4		NP 056982.1	HIV-1 inducer of short transcripts binding protein	205	39-52
			ÁAC72973.1	HIV-1 inducer of short transcripts binding protein	205	3e-52
NIM_008158		3 (+			
		U:(C-IR)				
NP_032184.1 Mm.35009 2.05	Mm.35009	2.05	NP_061844.1	G protein-coupled receptor 27; super conserved receptor expressed in brain 1	453	e-127
	: :	, ,	\	GP27_HUMAN Probable G protein-coupled receptor GPR27 (Super conserved	·	
			69NS67	receptor expressed in brain 1)	453	e-127
	i		JC7287	G-protein coupled receptor, SREB1	453	e-127
			BAA96645.1	SREB1	453	e-127
			AAH30577.1	similar to G protein-coupled receptor 85	249	, 5e-66
			NP_061843.1	G protein-coupled receptor 85, super conserved receptor expressed in brain 2	. 248	2e-65
			O9NPD1	GP85_HUMAN Probable G protein-coupled receptor GPR85 (Super conserved recentor expressed in brain 2) (PK+Cx1)	248	28-65
			T47131	G-protein coupled receptor, SREB2	248	
			CAB82307.1	hypothetical protein	248	2e-65
		· .	BAA96646.1	SREB2	248	2e-65
,			AAF79956.1	AF250237 1 orphan G protein-coupled receptor 85	248	2e-65

			BAC05911.1	seven transmembrane helix receptor	248	2e-65
	; ; ; ;	ţ	NP_061842.1	super conserved receptor expressed in brain 3	233	3e-61
-			99SN6O	SRB3_HUMAN Super conserved receptor expressed in brain 3	233	3e-61
			JC7289	G-protein coupled receptor, SREB3	233	3e-61
, see			BAA96647.1	SREB3	233	3e-61
		.3	AAH09861.1	AAH09861 super conserved receptor expressed in brain 3	233	3e-61
NM_019513 NP_062386.1	Mm.1170 15	U:(C-IR) 2.05	NP_009151.1	carbonic anhydrase VB, mitochondrial precursor; carbonic dehydratase	. 605	e-173
		,	Q9Y2D0	CASB_HUMAN Carbonic anhydrase VB, mitochondrial precursor (Carbonate dehydratase VB) (CA-VB)	605	e-173
			BAA76671.1	carbonic anhydrase VB	605	e-173
, ;			AAH28142.1	carbonic anhydrase VB, mitochondrial	605	e-173
			NP_001730.1	carbonic anhydrase VA, mitochondrial precursor; carbonic anhydrase V, mitochondrial; carbonic dehydratase	384	24 901-9
			P35218	CAH5_HUMAN Carbonic anhydrase VA, mitochondrial precursor (Carbonate dehydratase VA) (CA-VA)	384	e-106
			CRHUS	carbonate dehydratase (EC 4.2.1.1) V precursor [validated]	384	e-106
		-	AAA02890.1	carbonic anhydrase V	384	e-106
			AAB47048.1	carbonic anhydrase V; CA V	384	e-106
		;	AAC99806.1	carbonic anhydrase V	384	e-106
			1UGD	Human Carbonic Anhydrase Ii[hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s)	286	4e-77
			IUGG	Human Carbonic Anhydrase Ii[hcaii] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s) - Orthorhombic Form	286	4e-77
	:		1UGF	Human Carbonic Anhydrase Ii [hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Thr (A65t)	285	9e-77
			1G52	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,3-Difluorophenyl)methyl]-Benzamide	285	9e-77
			1654	A Chain A, Carbonic Anhydrase I'i Complexed With [4.(Aminosulfonyl)-N-[(2,3,4,5,6-Pentafluorophenyl)methyl]-Benzamide	285	9e-77

	<u> </u>	1	16	<u> </u>	16		225	T ~	T	T	1 -	· 1 -	1 .	15				_
	96-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	9e-77	96-77	96-77	
	285	285	285	285	285	285	285	285	285	285	285	285	285	285	285	285	285	
	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6629 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 2-(3-Methoxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-Fluorobenzenesulfonamide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,6-Difluorophenyl)methyl]-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With (S)-N-(3-Indol-1-YI-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With (R)-N-(3-Indol-1-Y1-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With Al-8520 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 4-Amino-3,4-Dihydro-2-(3-Methoxypropyl)-, 1,1-Dioxide, ®	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6619 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 2-(3-Hydroxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	A Chain A, Carbonic Anhydrase Ii Complexed With 2,6-Diffuorobenzenesulfonamide	A Chain A, Carbonic Anhydrase Ii Complexed With N-[2-(1h-Indol-5-YI)-ButyI]-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2-Fluorophenyl)methyl]-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With 3,5-Diffuorobenzenesulfonamide	Carbonic Anhydrase Ii Inhibitor: Acetohydroxamate	A Chain A, The Mechanism Of Cyanamide Hydration Catalyzed By Carbonic Anhydrase Ii Revealed By Cryogenic X-Ray Diffraction	Carbonic Anhydrase Ii Complex With The 10km Inhibitor 4-Sulfonamide-[1-(4-Aminobutane)]benzamide	Carbonic Anhydrase Ii Inhibitor	Carbonic Anhydrase Ii Inhibitor	Carbonic Anhydrase Ii Inhibitor	Carbonic Anhvotrase Ii Inhihitor
	118Z	1IF4	1G53	1压8	1IF7	1190	1191	1IF5	1压9	1GID	1IF6	1AM6	1F2W	10KM	1BN1	1BN4	1BN3	1RMM
			1					:	:		,			(*				
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	1 DATE			
		Cathonic Annydrase 11 Inhibitor	285	9e-77
- -	IBNM.	Carbonic Anhydrase Ii Inhibitor	285	9e-77
	1CIL	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complexed With The Inhibitor Ets	285	
	2CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) Complex With Thiocyanate Ion	285	
	 3CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) Complex With 3-Mercuri-4-Aminobenzenesulfonamide (AMS).	285	9e-77
÷.	1CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1)	285	00-77
	1BNT	Carbonic Anhydrase Ii Inhibitor	285	·
.	1BNU	Carbonic Anhydrase Ii Inhibitor	285	96-77
	1A42	Human Carbonic Anhydrase Ii Complexed With Brinzolamide	285	9e-77
	1BNW	Carbonic Anhydrase Ii Inhibitor	285	22
:	1BNQ	Carbonic Anhydrase Ii Inhibitor	285	9e-77
	10KN	Carbonic Anhydrase Ii Complex With The 10kn Inhibitor 4-Sulfonamide-[1-(4-N-(5-Fluorescein Thiourea)butane)]	285	9e-77
	10KL	Carbonic Anhydrase Ii Complex With The 1old Inhibitor 5-Dimethylamino-Naphthalene-1-Sulfonamide	285	9e-77
	1CRA	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With 1,2,4-Triazole	285	9e-77
	 1CA0	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Hydrogen Sulfide	285	9e-77
	2CBA	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, Ph 7.8)	285	9e-77
	2CBD	Carbonic Anhydrase Ii (E.C.4.2,1.1) (2.4 M Ammonium Sulfate, 0.3 M Sodium Bisulfite, Ph 7.3)	285	9e-77
	2CBB	Carbonic Anhydrase Ii (E.C.4.2.1.1) (80 Mm Sodium Citrate, 2.4 M Ammonium Sulfate, Ph 6.0)	285	9e-77
	1RAY	Carbonic Anhydrase II (E.C.4.2.1.1) Complex With Azide	285	9e-77
	IRZB	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By By Cobalt(II) At Ph 6.0	285	9e-77
	2CBE	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 2mm Dipicolinate, Ph 7.8)	285	9e-77
	2CBC	Carbonic Anhydrase Ii (E.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 0.2 Formate, Ph 7.6)	285	9e-77

			1САН	Carbonic Anhydrase Ii (E.C.4.2.1.1) (Native Zinc Replaced By Cobalt) Complex With	285	9e-77
		:	1RZC	Outhouse Antimone If (D C 4 o 4 1) trees of the contraction of the con		
			TBCT	Caround Author 11 (D. C. 4.2.1.1) With Ame Replaced By Copper(II)	285	9e-77
			יייייייייייייייייייייייייייייייייייייי	Carbonic Annyotase II (E.C.4.2.1.1) Complex With Trifluoromethane Sulphonamide	285	9e-7:7
			IKAZ	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Bromide	285	9e-77
			1RZA	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By Cobalt(Ii)	285	9e-77
			1RZD	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By Manganese(Ii)	285	9e-77
		.\	1RZE	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By Nickel(Ii)	285	9e-77
\(\)			1CAY.	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Acetate	285	9e-77
	,		5CAC	Carbonic Anhydrase Form C (E.C.4.2.1.1) Complex With Hydrogen Sulfite	285	0° 77
	1	·	4CAC	Carbonic Anhydrase Form C (E.C.4.2.1.1) (Ph 6)	285	0P-77
		ï	1BV3	A Chain A, Human Carbonic Anhydrase Ii Complexed With Urea	285	22
		,	1AVN	Human Carbonic Anhydrase Ii Complexed With The Histamine Activator	205	
	:		1LZV	A Chain A, Site-Specific Mutant (Tyr7 Replaced With His) Of Human Carbonic	285	9e-77
			NP 000058 1	control orderdrone II. sometime II. 1. 1. Tr. 1		
	1		1.900000	varbounc aunyutase II; carbonate denydratase II; carbonic dehydratase; carbonic anhydrase B	. 285	9e-77
			D00019	CALLS THIRANN C. 1		•
		·	1,00910	CARL_HUMAIN Carbonic anhydrase II (Carbonate dehydratase II) (CA-II) (Carbonic anhydrase C)	285	9e-77
		,	CRHU2	carbonate dehydratase (EC 4.2.1.1) II [validated]	285	9e-77
1		÷	1EOU	A Chain A, Crystal Structure Of Human Carbonic Anhydrase Ii Complexed With An Anticonvulsant Sugar Sulfamate	285	9e-77
	·	:	1CNX	Mol_id: 1; Molecule: Carbonic Anhydrase Ii; Chain: Null; Synonym: Carbonate Dehydratase, Hca Ii: Ec: 4.2.1.1: Heterogen: Benzenesulfmamida	. 285	9e-77
	1		1CNW	Mol_id: 1; Molecule: Carbonic Anhydrase Ii; Chain: Null; Synonym: Carbonate Dehydratase, Hca Ii; Ec: 4.2.1.1; Heterogen. Ethylaminocarbonylhenzenesulfunamide	285	9e-77
			1CNY	Mol_id: 1; Molecule: Carbonic Anhydrase II; Chain: NuII; Synonym: Carbonate Dehydratase, Hca II; Ec: 4.2.1.1; Heterogen, Aminocarbonylbenzenesulfonamide	285	9e-77
			4CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1)	285	9P-77
			1CA3	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) (pH 5.7)	285	9e-77
•					- 333	1

			11101			
			IHCA	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) (pH 6.5)	285	9e-77
			CAA68426.1	carbonic anhydrase II (AA 1-260)	285	9e-77
		1	AAA51908.1	carbonic anhydrase II	285	9e-77
			AAA51909.1	carbonic anhydrase II	285	96-77
			ÄÄA51911.1	carbonic anhydrase II	285	9e-77
-			1UGB	Human Carbonic Anhydrase Ii[hcaii] (E.C.4.2.1.1) Mutant With Ala 65 Replaced By Gly (A65g)	285	1e-76
			1LG5	A Chain A, Crystal Structure Analysis Of The Hca Ii Mutant T199p In Complex With Beta-Mercaptoethanol	285	1e-76
(1		· · · · · · · · · · · · · · · · · · ·	1LG6	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Thiocyanate	285	1e-76
			1LGD	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Bicarbonate	285	16-76
NM_008890		U:(C-R)				
NP 032916.1	Mm.57030	2.04	NP_002677.1	phenylethanolamine N-methyltransferase	462	e-130
			P11086	PNMT_HUMAN Phenylethanolamine N-methyltransferase (PNMTase) (Noradrenaline N-methyltransferase)	462	e-130
			A28171	phenylethanolamine N-methyltransferase (EC 2.1.1.28)	462	e-130
		1	1HNN	B Chain B, Crystal Structure Of Human Pnmt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
			1HNN	A Chain A, Crystal Structure Of Human Pumt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
3 1 3 1 1	-		AAA60130.1	phenylethanolamine N-methyltransferase	462	e-130
		:	CAA36944.1	phenylethanolamine n-methyltransferase	462	e-130
	i		AAH37246.1	phenylethanolamine N-methyltransferase	462	e-130
	· ; '		AAA60131.1	phenylethanolamine N-methyltransferase	461	e-130
NM_008985 NP_033011.1	Mm.2902	U:(C-IR) 2.04	NP 002837.1	protein tyrosine phosphatase, receptor type, N precursor; islet cell antigen 2; islet cell antigen 512; islet cell autoantigen 3; protein tyrosine phosphatase-like N precursor	1389	0

								22	9			_		-							
	0			0		e-173	e-173	e-173	. 6 173	e-173	e-173	e-173	e-173	e-173	e-173	151	e-164	e-152	-	0.150	201-0
1389	1389	0770	02.5	850	:	607	607	209	. 607	209	. 607	209	209	209	209	670	570	481		181	2005
PTPN_HUMAN Protein-tyrosine phosphatase-like N precursor (R-PTP-N) (PTP IA-2)(Islet cell antigen 512) (ICA 512) (Islet cell autoantigen 3)	tyrosine phosphatase	Islet Cell Antigen 512	AAH07713 protein tyrosine phosphatase, receptor type, N	islet cell antigen 512		protein tyrosine phosphatase recentor ni	I come of come procedures a configuration of the co	protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 1 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	PTPX_HUMAN Protein-tyrosine phosphatase X precursor (R-PTP-X) (Islet cell autoantigen related protein) (ICAAR) (IAR) (Phogrin)	phogrin precursor	phogri	transmembrane tyrosine phosphatase-like protein, ICAAR	Islet Cell Autoantigen Releted	IAR/receptor-like protein-tyrosine phosphatase precursor	KIAA0387	protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 3 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	protein tyrosine phosphatase, receptor type, N polypeptide 2	odd-skipped-related 2A protein		unnamed protein product	AAH16936 odd-skipped-related 2A protein
	AAA90974.1	CAA44688.2	AAH07713.1	I37577	NP 5708571	11 122		NP 002838.1	Q92932	JC5062	AAC50742.1	JC5263	CAA69880.	AAB63600.1	BAA20841.2	NP_570858.1	AAH34040.1	AAK74066.1		BAC11035.1	AAH16936.1
								, ·	-		;				•			U:(C-IR) 2.03	U:(C-IR) 2.46		
		-														,	1	1	Mm.4633 6		. ·
		,												; ·					NM 054049 NP 473390.1		

			NP 443727.1	443727.1 odd-skipped-related 2A protein	507	e-143
	i	,	AAK74067.1	odd-skipped-related 2B protein	507	e-143
			XP_059439.2	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	2e-95
			NP_660303.1	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	. 2e-95
		i	AAH25712.1	Similar to odd-skipped related 1 (Drosophila)	347	2e-95
		-	BAB92079.1	zinc finger transcription factor	347	2e-95
		. ,	BAC11079.1	unnamed protein product	347	2e-95
NM_007924	,	(1)				
NP_031950.1	Mm.1552	0:(C-1K) 2.03	NP 006523.1	ELL gene (11-19 lysine-rich leukemia gene)	880	0
			P55199	ELL_HUMAN RNA polymerase II clongation factor ELL (Eleven-nineteen lysine-rich leukemia protein)	880	230
	i gra		I38880	eleven-nineteen lysine-rich leukemia gene (ELL) protein	880	0
, V			AAA57120.1	BLL	880	0
	:		AAB34056.1	MEN chimeric transcription factor	803	0
			NP_036213.1	ELL-related RNA polymerase II, elongation factor	371	e-102
	. `	,	O00472	ELL2_HUMAN RNA polymerase II elongation factor ELL2	371	e-102
			AAC51232.1	RNA polymerase II elongation factor ELL2	371	e-102
			AAH28412.1	ELL-RELATED RNA POLYMERASE II, ELONGATION FACTOR	371	e-102
NM_008521		TT. (C. TD.)			·	
NP 032547,1	Mm,4088	0:(C-11K) 2,03	AAH29498.1	leukotriene C4 synthase	204	5e-53
	ji L		JC5398	leukotriene C4 synthase (EC 6)	204	7e-53
		:	NP_665874.1	leukotriene C4 synthase isoform 1	204	7e-53
1	. ,		Q16873	LC4S_HUMAN Leukotriene C4 synthase (Leukotriene-C(4) synthase) (LTC4 synthase)	204	7e-53
		·	I38595	leukotriene-C4 synthase (EC 2.5.1.37)	204	7e-53
,		:	AAA20467.1	leukotriene C4 synthase	204	7e-53

200:		3239										23 1	1						PC	J\T	J S2	00:	5/005596		
	, 7e-53	7e-53	7e-53	9e-95	0.05	20-06	ye-92	9e-95	9e-95	9e-95	2e-91	2e-91	2e-91	1e-90	e-148		e-148	e-148	e-148		4è-87	2e-84			
	204	204	204	345	315	215	040	345	345	345	333	333	333	331	522		522	277	222 445		319	310	000	3	066
1 miles of the second s			\neg	chymase 1, mast cell preproprotein; chymase, mast cell; chymase, heart; mast cell protease I	MCT1_HUMAN Chymase precursor (Mast cell protease I)	chymase (BC 3.4.21.39) precursor [validated]		_	oftennan	cuymase	Crystal Structure Of Pmsf-Treated Human Chymase At 1.9 Angstroms Resolution	chymase	chymase	A Chain A, The 2.2 A Crystal Structure Of Human Chymase In Complex With Succinyl-Ala-Pro-Phe-Chloromethylketone	ring finger protein 32	hypothetical protain	AF325690 1 FKSG33	AF441222 1 ting finger protein RNF32	AC005534 2 supported by human ESTs AA412402 (NID:g2070990) NH44021	(INID:g1182349), mouse EST AA065933 (NID:g1562789), and genscan	AAH13410 Similar to hypothetical protein DKFZp434C135	Similar to ring finger protein 32	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1; ecotropic retroviral receptor; Solute carrier family 7 (cationic amino acid transporter, y+ system),; amino acid transporter, cationic 1	CTR1_HUMAN High-affinity cationic amino acid transporter-1 (CAT-1) (CAT1) (System Y+ basic amino acid transporter) (Ecotropic retroviral leukemia receptor	homolog) (ERR) (Ecotropic retrovirus receptor homolog)
A A A 50555 1	A A C/50/176 1	A A DOCTO 1	AMB001/23.1	NF_001827.1	P23946	KYHUCM	AAA52019.1	AAA52020.1	A A 52021 1	1.120202021.1	IKLI	AAB26828.1	1914144A	1PJP	NP_112198.1	CAB66808.1	AAG50281.1	AAM18664.1	AAD43189.1	A ATT1541C 1	AAH13410.1	AAH28120.1	NP_003036.1		P30825
			(m 2).11	2.03								-			U:(C-IR) 2.03	1 4.3	1,						U:(C-R) 2.02		
				Mm.1252			•								Mm.8735 2.	10 / 10 / 10 / 10 / 10 / 10 / 10 / 10 /							Mm.5255		
		1	NM 010780	NP_034910.1											NM_021470 NP_067445.1					1			NM_007513 NP_031539.1		

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	980	8	988	886	654	654		878	040	640	2 9	049	630	637	421	411	411	202	3	303	3		330	330	330	330	330	2
refroviral recentor	Cationic amino acid transmeter	reconstruction and transported	TOUCHINI TOUCHT	KECIL	CTR2_HUMAN Low-affinity cationic amino acid transporter-2 (CAT-2) (CAT2)	cationic amino acid transporter 2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2; Solute	cather family / (canonic amino acid transporter, y+ system),; amino acid transporter, cationic 2	hCAT-2A	solute carrier family 7 (cationic amino acid transporter, v+ system). member 3	cationic amino acid transporter	unnamed protein product	solute carrier family 7 (cationic amino acid transporter, v+ system). member 3	unnamed protein product	unnamed protein product	similar to Cationic amino acid transporter-4 (CAT-4) (CAT4)	Unknown (protein for MGC:10733)	solute carrier family 7 (cationic amino acid transporter, v+ system) member 4	CTR4_HUMAN Cationic amino acid transporter-4 (CAT-4) (CAT4)	cationic amino acid transporter 3			epithelial V-like antigen 1 precursor	epithelial V-like antigen 1 precursor	EVA1_HUMAN Epithelial V-like antigen 1 precursor	epithelial V-like antigen precursor	AF275945_1 epithelial V-like antigen 1	AF304447 1 enithelial V_like anticen 1
CAA41869.1	AAC27721.1	\$29685	CA A 40.500 1	CAA40360.1	P52569	BAA06271.1		NP 003037.1	AAB62810.1	NP_116192.2	AAL37184.1	BAC11353.1	AAH33816.1	BAC11253.1	BAB55118.1	XP 036892.1	AAH08814.1	NP_004164.1	043246	CAA04263.1	1		NF 005/88.1	NP_658911.1	060487	AAC39762.1	AAF87240.1	A A G 73183 1
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			L							٦٠		-6-	٩	2 2	5 6			P-115	P-115	e-115	2116	A-115	P-115	
330	420	757	77	420	420	420	420	418	418	418	418	418	418	416	416	415	414	413	412	412	412	412	412	
1 epithelial V-like antigen 1	1B05_HUMAN HLA class I histocompatibility antigen, B-13 B*1301 alpha chain precursor (B13.1)	MHC class I histocompatibility antigen HI A-B13 mecursor				7					HLA-B*1301 antigen	glycosylation aa 86, alpha domain 1 aa 1-24, alpha domain 2 aa 25-114, alpha domain 3 aa 207-298	MHC class I antigen	MHC class I lymphocyte antigen		MHC antigen	MHC class I antigen HLA-B precursor	lymphocyte antigen	HLA class I antigen HLA-B	1B32_HUMAN HLA class I histocompatibility antigen, B-39 B*3902 alpha chain	MHC class I histocompatibility antigen precursor		MHC class I antigen	(FILK ninnel family member CITO instantation Later
AAH17774.1	P30461	154442	AAA52657.1	AAA59660.1	BAA08822.1	CAC171361	CAC17127 1	A45850	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	AAA39627.1	BAA08821.1	AAA59618.1	CAC29063.1	AAÄ73509.1	AAD00010.1	AAB06829.1	AAA98506.1	I84488	AAC31793.1	P30476	I68850	AAA52659.1	AAA87396.1	NP 084656.1
	U:(C-IR) 2.02																							U:(C-R)
	Mm.1960 32					* ***								,										- 1
	NM 010393 NP 034523.1									1.5				• .										

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	1821	1810	1810	1810	1263		1263	1252		1252	1043	1043	1004	1004	1004	730	719	445	. 445	445	445	445	777
11.511.0	7	GLI-Kruppel family member GLI2 isoform alpha; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein	GLI2_HUMAN Zinc finger protein GLI2 (Tax helper protein)	hGLI2		 Jame Linger Protein CLLL; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein 	hGL12	· .	protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein	hGLI2	GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zinc finger protein GLI3	GLI3 protein	GLI3_HUMAN Zinc finger protein GLI3	190K DNA-binding protein GLJ3	DNA-binding protein	Tax helper protein 1	Tax helper protein 2	glioma-associated oncogene homolog	GLI1_HUMAN Zinc finger protein GLI1 (Glioma-associated oncogene) (Oncogene GLI)	transforming protein gli	GLI protein (AA 1-1106)	AAH13000 Similar to glioma-associated oncogene homolog (zinc finger protein)	GLII
BAA256661	100000000000000000000000000000000000000	NP_084655.1	P10070	BAA25665.1	NP_005261.1		BAA25668.1	NP_084657.1		BAA25667.1	NP_000159.2	CAB59315.1	P10071	A35927	AAA52564.1	BAA03568.1	BAA03569.1	NP_005260.1	P08151	TVHUGL	CAA30297.1	AAH13000.1	AAM13391.1 GLI1
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٠.		U:(C-IR)	BAA19667.1	Similar to Rat growth factor Arc (U19866)	765	0
NM_018790 NP_061260.1	Mm.2540 1 5	U:(C-D) 2.34	į			,
		,	NP_056008.1	activity-regulated cytoskeleton-associated protein	763	C
	:		AAF07185.1	AF193421_1 ARC	763	. .
			AAG33705.1	AF248637_1 activity-regulated cytoskeleton-associated protein	763	
		·	AAH12321.1	AAH12321 Similar to activity-regulated cytoskeleton-associated protein	763	
		U:(C-R)	NP_066013.1		2055	
NM_020043 NP_064427.1	Mm.1437 41	U:(C-D) 2.17				,
	·		BAB86306.1	hDDM36	2055	235
			BAB13454.1	KIAA1628 protein	1539	0
	- 7		AAC51287.1	neogenin	260	20-6
			NP_002490.1	neogenin homolog 1 (chicken); neogenin (chicken) homolog 1	260	
	,		092859	NEO1_HUMAN Neogenin precursor	260	2e-68
		1	AAB17263.1	neogenin	260	2e-68
			NP_005206.1	deleted in colorectal carcinoma	226	2e-58
			P43146.	DCC_HUMAN Tumor suppressor protein DCC precursor (Colorectal cancer suppressor)	226	2e-58
			A54100	tumor suppressor protein DCC precursor	226	26-58
:			CAA53735.1	fumour suppressor	226	
***	,		AAA35751.1	colorectal tumor suppressor (put.); putative	216	3e-55
	-; !	U:(C-IR)	Q9UP79	ATS8_HUMAN ADAMTS-8 precursor (A disintegrin and metalloproteinase with	1404	0
NM_013906 NP_038934.1	Mm.1005 82	U.(C-D) 2.16		uncomosponum motas e) (ALAM-15 8) (ALAM-158) (METH-2) (METH-8)		
			AAD48081.1	AF060153_1 METH2 protein	1404	٩
			NP 008968.2	a disintegrin and metalloprotease with thrombospondin motifs-8	1403	٥

				·				23	90						:									
0	0	0	0	0	0	0	0	0	0	e-154	· e-154	e-154	e-154	e-119	e-119	3e-87	1e-74	1e-74	1e-74	1e-70	1e-69	1e-69	1e-69	
799	799	799	798	798	798	798	795	733	733	543	543	543	543	426	426	321	279	279	279	266	263	263	262	3
a disintegrin and metalloprotease with thrombospondin motifs-1 preproprotein; human metalloproteinase with thrombospondin type 1 motifs	1 AF207664_1 matrix metalloprotease	1 metalloprotease with thrombospondin type 1 motifs	1 AF060152_1 METH1 protein	ATS1_HUMAN ADAMTS-1 precursor (A disintegrin and metalloproteinase with thrombospondin motifs 1) (ADAM-TS1) (ADAM-TS1) (METH-1)			1 Unknown (protein for MGC:32979)	a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 15 preproprotein	I metalloprotease disintegrin 15 with thrombospondin domains		1 DKFZP586G1122 protein	AF304052_1 hematopoietic zinc finger protein	1 DKFZP586G1122 protein	hypothetical protein DKFZp586G1122.1	l hypothetical protein	unnamed protein product	1 hypothetical protein FLJ22419	unnamed protein product	1 AAH07212 hypothetical protein FLJ22419	unnamed protein product	1 hypothetical protein FL125270	umamed protein product	similar to zinc finger protein 385; hematopoietic zinc finger	8422.1 Invnothetical protein FI 195270
NP_008919.2	AAF23772.1	BAA95502.1	AAD48080.1	Q9UHI8	AAF15317.1	BAA92584.1	AAH36515.1	NP_620686.1	CAC86014.1	XP_028643.4	NP_056296.1	AAL08625.1	AAH29752.1	T17248	CAB55938.1	BAB14910.1	NP 078973.1	BAB15350.1	AAH07212.1	BAC04870.1	NP 689733.1	BAB71629.1	XP_087103.1	AAH38422.1
٠		5								U:(C-IR) 2.01						÷							·	
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		,								NM_013866 NP_038894.1							1,			,	·			

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1271	1271	1271	1271	1271	243	237	237	237	237	232	232	228	228	225	225	225	222	222	222	222	222	222	992
009114.1 plakophilin 3	PKP3_HUMAN Plakophilin 3	płakophilin 3	AF053719_1 plakophilin-3 protein	AAH00081 plakophilin 3	plakophilin 2a	arm-repeat protein NPRAP/neurojungin	GT24	catenin (cadherin-associated protein), delta 2 (neural plakophilin-related arm-repeat protein); catenin (cadherin-associated protein), delta 2	neural plakophilin-related arm-repeat protein (NPRAP)	CTD2_HUMAN Catenin delta-2 (Delta-catenin) (Neural plakophilin-related ARM-repeat protein) (NPRAP) (Neurojungin) (GT24)	delta-catenin	band-6-protein	band-6-protein	plakophilin 1; Plakophilin-1	plakophilin	plakophilin 1	plakophilin 2	PKP2_HUMAN Plakophilin 2	plakophilin 2b	plakophilin 4	PKP4_HUMAN Plakophilin 4	p0071 protein	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18; cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase
	Q9Y446	CAB44310.1	AAF23050.1	AAH00081.1	CAA66265.1	AAB97957.1	AAD00453.1	NP_001323.1	BAA36163.1	Q9UQB3	AAC63103.1	S60712	CAA55881.1	NP_000290.1	CAA84426.1	CAA98022.1	NP_004563.1	099959	CAA66264.1	NP_003619.1	099569	CAA57478.1	NP_000763.1
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Mm.2960 U:(C-IR) NP_3	:					: :					. : .) \			:		-			Mm.1425 81
NM_019762 NP_062736.1						A	:															,	NM_028089 NP_082365.1

			AAB59356.1	Cytochrome		
, 1	•		P33260	CPCI HIIMAN (Attochrome D450 2019 (OXDITC19) (B450 CE 100)	766	0
			461260	C. C. T. C.	764	0
			4 4 4 00 00 4	cynomome r450 2C18	764	0
			AAA02050.1	cytochrome P-4502C18	764	0
.			ш.	cytochrome P-450	736	0
-		:	NP_000762.2	cytochrome P450, subfamily IIC, polypeptide 9; cytochrome P450, subfamily IIC	736	
1				(mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase;		•
				monooxygenase		<u> </u>
		t.	P11712	CPC9_HUMAN Cytochrome P450 2C9 (CYPIIC9) (P450 PB-1) (P450 MP-4)	736	0
			B38462	S-mephenytoin 4-hydroxylase (RC 114.14.1) withouthouse 19450.200	Ì	
·,		۱.	1313295A	extroducing DASO	736	0
			D 4 4 00102 1	cytocatomic 1450	736	0
			BAAUU123.1	cytochrome P-450	. 736	0
			P11713	CPCA_HUMAN Cytochrome P450 2C10 (CYPIIC10) (P450 MP-8) (S-mephenytoin 4-hydroxylase) (P-450MP)	729	0
		,	D28951	cytochrome P450 2C10	770	
			AAA52157.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	72.9	
			AAA52158.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	720	2 6
			1506290A	cytochrome P450	77.8	
	;		NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase) nolynentide 10.	77.6	
				mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	07/)
			P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYPIIC19) (P450-11A) (Mephenytoin	726	
				4-hydroxylase) (CYPIIC17) (P450-254C)	3	,
			AAB59426.1	cytochrome	726	0
			F38462	S-mephenytoin 4'-hydroxylase (EC 1.14.14) cytochrome P450 2C19	722	C
		U:(C-IR)	CAA11218.1	36 kDa phosphothyrosine protein	231	2e-60
NM_010689 NP_0348191	Mm.1028 0	U:(C-D)				
1.710.00	2	7.7				

		ī	AAC39636.1 LAT	LAT	231	20,60
			AAH11563.1	AAH11563 Similar to linker for activation of T cells	22.1	20,00
		•	NP_055202.1	linker for activation of T cells	210	79-97
			043561	LAT_HUMAN Linker for activation of T cells (36 kDa phospho-tyrosine adaptor protein) (m36) (n36-38)	215	16-55
			AAC39637.1	LAT	215	10.55
NM_017370 NP_059066.1	Mm.2673 0	U:(C-D) 6.81	CAA25926.1	haptoglobin	665	e-171
			P00737	HPT1_HUMAN Haptoglobin-1 precursor	508	171
		,	HPHU1	haptoglobin precursor, allele 1 [validated]	598	P-171
			AAA52684.1	preprohaptoglobin	20%	P.171
	·		CAA25267.1	haptoglobin alpha 1S	20%	239
			AAC27432.1	haptoglobin	597	π
			NP_066275.2	haptoglobin-related protein; Haptoglobin-related locus	5,69	6-160
	,		P00739	HPTR_HUMAN Haptoglobin-related protein precursor	569	e-162
			HPHUR	haptoglobin-related protein precursor	569	e-162
		1	AAA88079.1	haptoglobin-related protein	569	e-162
			AAA88081.1	haptoglobin-related protein	569	e-162
			CAA25927.1	haptoglobin	568	e-162
	,		AAC27433.1	haptoglobin-related protein precursor	565	e-161
	•		CAA61501.1	haptoglobin-related protein	565	e-161
			AAA52687.1	haptoglobin precursor	559	e-159
		Ş	NP_005134.1	haptoglobin	559	e-159
		·	P00738	HPT2_HUMAN Haptoglobin-2 precursor	559	e-159
			HPHU2	haptoglobin precursor, allele 2	559	e-159
			$\neg \neg$	haptoglobin precursor	559	e-159
		, , , , , , , , , , , , , , , , , , ,	AAA88078.1	haptoglobin	559	e-159
			AAA88080.1	haptoglobin	559	e-159

						,
			AAA52685,1	preprohaptoglobin	559	e-159
			1006264A	haptoglobin Hp2	508	e-144
NM_007424		U:(C-D) 4.11 U:(R-D)		aggrecan 1 isoform 2 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identifies by monoclonal antibody A0122).	·	
NP_031450.1	Mm.2759	3.08	NP_037359.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1795	
				aggrecan 1 isoform 1 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identifies by monoclonal antibody A0122):		
			NP_001126.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1794	0
			AAA62824.1	large aggregating cartilage proteoglycan core protein	1794	0
		- 1	A39086	aggrecan precursor, cartilage long splice form	1792	0
			AAH36445.1	Similar to aggrecan 1 (chondroitin sulfate proteoglycan 1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122)	1253	0
			CAA35463.1	cartilage specific proteoglycan (600 AA)	823	0
	* · · · · · · · · · · · · · · · · · · ·	12.00	AAA35726.1	profeoglycan core protein	573	e-162
			AAH10571.1	chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101
			AAG23134.1	AF228710_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101
			AAG23135.1	AF229053_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	. e-101
NM_009008	Vim 1072	U.(C-D)	100000 CIV	ras-related C3 botulinum toxin substrate 2; Ras-related C3 botulinum toxin substrate 3 (tho family, small GTP-binding protein Rac2); rho family, small GTP binding protein		
T*+COCCO TAT		7.07	INF_002003.1	Kacz	390	e-108
	÷		P15153	RAC2_HUMAN Ras-related C3 botulinum toxin substrate 2 (p21-Rac2) (Small G protein) (GX)	390	e-108
			B34386	GTP-binding protein rac2	390	e-108
	i î		1DS6	A Chain A, Crystal Structure Of A Rac-Rhogdi Complex	390	e-108
			AAA36538.1	ras-related C3 botulinum toxin substrate	390	e-108
	:		AAB22207.1	rac1 p21≕small GTP-binding protein [human, HL60, Peptide, 192 aa]	390	e-108
			CAB45265.1	dJ151B14.2 (ras-related C3 botulinum toxin substrate 2 (rho family, mall GTP binding protein Rac2))	390	e-108
			AAH01485.1	AAH01485 ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	390	e-108

				COLOR III MANUEL TILL THE TOTAL TOTA		
				rac_related (13 hoth) limin towin milrated 1 . C. T.	390	e-108
			NP_008839.2	nas-react C2 bottumum toxm substrate 1 isotorm Rac1; rho family, small GTP binding protein Rac1	367	e-101
	, .		P15154	RAC1_HUMAN Ras-related C3 botulinum toxin substrate 1 (p21-Rac1) (Ras-like protein TC25)	798	101
•	:		TVHUC1	GTP-binding protein rac1	367	e-101
			114D	D Chain D, Crystal Structure Analysis Of Rac1-Gdp Complexed With Arfaptin (P21)	367	e-101
			114L	D Chain D, Crystal Structure Analysis Of Rac1-Gdp In Complex With Arfaptin (P41)	. 367	e-101
		:	AAA36537.1	ras-related C3 botulinum toxin substrate	367	e-101
			22206.1	rac1 p21=small GTP-binding protein [human, HL60, Peptide, 192 aa]	367	e-101
i i			CAB53579.5	Rac1 protein	367	e-101
	<u>.</u>		AAM21111.1	AF498964_1 small GTP binding protein RAC1	367	e-101
7	٠.		AAH04247.1	AAH04247 ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	367	-101
			AAA35941.1	small G protein	366	e-101
		.,	AAA36544.1	ras-like protein	366	e-101
			114T	D Chain D, Crystal Structure Analysis Of Rac1-Gmppnp In Complex With Arfaptin	365	e-100
1 N			1e+96	1e+96 A Chain A, Structure Of The RacP67PHOX COMPLEX	363	e-100
	ì		1HH4	A Chain A, Rac1-Rhogdi Complex Involved In Nadph Oxidase Activation	362	e-100
			1HH4	B Chain B, Rac1-Rhogdi Complex Involved In Nadph Oxidase Activation	362	e-100
	1 1		NP_005043.1	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3); rho family, small GTP binding protein Rac3	358	16-98
		·	∞	RAC3_HUMAN Ras-related C3 botulinum toxin substrate 3 (p21-Rac3)	358	1e-98
	:		AAC51667.1	Rac3	358	1e-98
			AAH15197.1	AAH15197 ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	358	16-98
	· ; · ·		AAH09605.1	AAH09605 ras-related C3 botulinum toxin substrate 3 (tho family, small GTP binding protein Rac3)	358	16-98
			AAM21113.1	AF498966 1 small GTP binding protein RAC3	358	16-98

						,
			NP_061485.1	ras-related C3 botulinum toxin substrate 1 isoform Rac1b; rho family, small GTP binding protein Rac1	356	56-98
1		er e men	CAA10732.1	small GTPase rac1b	356	1
x.*			AAD30547.1	AF136373_1 ras-related C3 botulinum toxin substrate isoform	356	
			CAA10733.6	Rac1b protein	356	
AK013740						
BAB28979.1	Mm.27579	U:(C-D) 2.82	NP_068747.1	hypothetical protein FLJ22649 similar to signal peptidase SPC22/23	298	. 1e-80
		·	BAB15437.1	unnamed protein product	298	1e-80
•			Q9H0S7	SP22_HUMAN Microsomal signal peptidase 23 kDa subunit (SPase 22 kDa subunit)	295	9e-80
		;	CAB66595.1	hypothetical protein	295	96-80
, , , , , , , , , , , , , , , , , , ,		(O.	NP_004346.1	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II	226	46-59
X00496 CAA25191.1	Mm.7043	2.81	•	antigen-associated); CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)		
		ŕ	CAA25192.1	putative p33	226	4e-59
			AAA36033.1	cell surface glycoprotein	226	4e-59
			AAH18726.1	AAH18726 CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	226	46-59
*		-	HLHUG	class II histocompatibility antigen-associated gamma chain	226	4e-59
	, .		CAA25193.1	putative p33	226	4e-59
	:		AAA36304.1	class II antigen gamma chain	226	4e-59
			CAA27047.1	gamma chain	225	9e-59
1-	•		P04233	HG2A_HUMAN HLA class II histocompatibility antigen, gamma chain (HLA-DR antigens associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD74 antigen)	207	16-53
	:	U:(C-D)	AAH36390.1	UDPN-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	1078	0
NM_015737 NP_056552.1	Mm.5699	U:(R-D) 2.1		1 (Call Call Call Call Call Call Call Cal		

	_ i _ i -	polypeptide N-acetylgalactosaminyltransferase 4; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4; GalNAc transferase 4; UDP-GalNAc; polypeptide N-acetylgalactosaminyltransferase 4; protein-UDP acetylgalactosaminyltransferase 4	1073	0
	< T	UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase	1073	0
	CAC80100.2	UDP-GalNAc-transferase 12	624	e-178
. 3 0	NP_078918.2	hypothetical protein FLJ21212; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12(GalNAc-T12)	622	e-178
* }	BAC07181.1	UDP-IN-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	622	e-178
	NP_004473.1	polypeptide N-acetylgalactosaminyltransferase 3; protein-UDP acetylgalactosaminyltransferase	462	e-130
	CAA63371.1	UDP-GaINAc:polypeptide N-acetylgalactosaminyltransferase (GaINAc-T3)	462	e-130
	AAH35822.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6)	461	e-129
	BAC11118.1	unnamed protein product	461	e-129
	NP_009141.1	polypeptide N-acetylgalactosaminyltransferase 6; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6; UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 6; protein-UDP acetylgalactosaminyltransferase 6; GalNAc transferase 6	459	e-129
	CAA69876.1	UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase	459	e-129
	BAB67811:1	KIAA1918 protein	417	e-116
	NP_065207.2	polypeptide N-acetylgalactosaminyltransferase 1; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1; GalNAc-T1; GalNAc transferase 1; protein-UDP acetylgalactosaminyltransferase 1; UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 1	416	e-116
	Q10472	PAGT_HUMAN Polypeptide N-acetylgalactosaminyltransferase (Protein-UDP acetylgalactosaminyltransferase) (UDP-GalNAc;polypeptide, N-acetylgalactosaminyltransferase) (GalNAc-T1)	416	e-116
	JC4223	polypeptide N-acetylgalactosaminyltransferase (EC 2.4.1.41)	416	e-116
	CAA59380.1	UDP-GalNAc:polypeptide N-acetylgalactosaminyl transferase	416	e-116

		e-139			e-138				e-134	e-132	e-129	e-123	e-123	e-123	e-121	e-108	e-108			e-107	P_107
		494	490	490	490	490	489	478	476	470	460	441	439	439	434	390	390	387	386	386	386
		alpha1-antichymotrypsin	similar to Alpha-1-antichymotrypsin precursor (ACT)	AACT_HUMAN Alpha-1-antichymotrypsin precursor (ACT)	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitypsin), member 3	Unknown (protein for MGC:18102)	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitypsin), member 3	alpha-1-antichymotrypsin precursor	alpha-1-antichymotrypsin precursor	alpha-1-antichymotrypsin precursor	A Chain A, Alpha1-Antichymotrypsin Serpin In The Delta Conformation (Partial Loop Insertion)	chymotrypsin inhibitor	alpha-1-antichymotrypsin, precursor, alpha-1-antichymotrypsin; antichymotrypsin	alpha-1-antichymotrypsin	A Chain A, Alpha1 Antichymotrypsin	AAH07920 Unknown (protein for MGC:14111)	L76133_1 lymphocyte antigen	AAH08403 Similar to major histocompatibility complex, class II, DR beta 5		MHC class II histocompatibility antigen DR beta 1 chain precursor	
		CAA48671.1	XP_028322.1	P01011	AAH03559.1	AAH10530.1	AAH34554.1	AAD08810.1	THUC	AAA51560.1	10MN	1313184C	NP-001076.1	AAA51543.1	2ACH	AAH07920.1	AAL40069.1	AAH08403.1	CAC08827.1	I54448	AAA59713.1
U:(C-D) 2.65	U:(C-D)							, ,	-		iv v			1		U:(C-D) 2.59					
Mm.1011 6		Min.14191		·											3	Mm.2256 4	Î				
NM_018866 · NP_061354.1	NM_008458	NP 032484.1				-										NM_010382 NP_034512.1	, ,				

			CAC08823.1	MHC class II antigen	386	e-107
			P20039	HB2I_HUMAN HLA class II histocompatibility antigen, DR-5 beta chain precursor	385	e-107
		;:	A25324	class II histocompatibility antigen HLA-DR-5 beta chain precursor	385	e-107
			AAA36274.1	MHC HLA DR5 cell surface glycoprotein beta chain precursor	385	e-107
	-	:	CAC08826.2	MHC class II antigen	385	e-107
			P13760	HB2H HUMAN HLA class II histocompatibility antigen, DR-4 beta chain precursor (DRB1*0401)	385	e-107
			A29310	MHC class II histocompatibility antigen HLA-DR beta 1 chain DR4 precursor	385	e-107
	. :		CAC19360.1	d1863G3.2 (major histocompatibility complex, class II, DR beta 1)	385	e-107
		·	CAB75359.1	human leucocyte antigen DRB1	385	e-107
			P01912	HB2B_HUMAN HLA class II histocompatibility antigen, DR-1 beta chain precursor (Clone P2-beta-3)	385	e-107
				pir HLHU3D MHC class II histocompatibility antigen HLA-DR beta 1 chain DR17 precursor	385	e-107
	i .	·	CAA25295.1	precursor	.385	e-107
			CAB06490.1	dJ93N13.3 (major histocompatibility complex, class II, DR beta 1 (clone P2-beta-3))	385	e-107
2	r.					
AK012581 -		-				
XP_126675.1	U:(C Mm.21687 2.55	U:(C-D) 2.55	AAK67634.1	Ixpothetical protein SB143	240	
			NP 085053.1	hypothetical protein MGC10986	240	2e-63
			AAH04400.1	Unknown (protein for MGC:10986)	240	2e-63
		-	BAC03855.1	unnamed protein product	240	2e-63
	· ·	U:(C-D) 2.47	NP_690591.1	membrane-spanning 4-domains, subfamily A, member 6A isoform 1; CD20-like precusor; membrane-spanning 4-domains, subfamily A, member 6: four-snan	233	5e-61
NM_027209 NP_081485.1	Mm.2948 7			transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso		
			AAG41780.1	AF212240 1 CDA01	233	5e-61
			AAK37417.1	AF237908 1 MS4A6A protein	. 233	5e-61
	,					

			4 A V7 2 7 0 0 4 4	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		
			1.4.4.1	ALZOUGOU_1 IND-FAUX-pulymotpul	233	26-61
		,	AAH22854.1	membrane-spanning 4-domains, subfamily A, member 6A	232	8e-61
			AAL56222.1	AF350502_1 four-span transmembrane protein 3.1	229	5e-60
		V	AAG44626.1	AF253977_1 HAIRB-iso	222	1e-57
			NP_071744.2	membrane-spanning 4-domains, subfamily A, member 6A isoform 2; CD20-like	208	1e-53
	. \		-: 	precusor; membrane-spanning 4-domains, subfamily A, member 6; four-span		
7				transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso		
			AAL07357.1	AF554930_1 MS4A6A	208	1e-53
		-	AAG27920.1	AF142409_1 CD20-like precusor	207	2e-53
			AAL56223.1	AF350503_1 four-span transmembrane protein 3.2	207	4e-53
NM_011116 NP_035246.1	Mm.6483	U:(C-D) 2.45	AAH36327.1	Similar to phospholipase D3	068	240
			AAH00553.1	AAH00553 similar to vaccinia virus HindIII K4L ORF	818	0
			NP_036400.1	similar to vaccinia virus HindIII K4L ORF	816	0
	,	;	AAB16799.1	HU-K4	816	0
			NP_620145.1	hypothetical protein BC015003	385	e-106
\(\frac{1}{2}\)			AAH15003.1	AAH15003 Unknown (protein for MGC;23565)	385	e-106
		* * * * * * * * * * * * * * * * * * * *	NP_689879.1	hypothetical protein FLJ40773	275	2e-73
			BAC05230.1	unnamed protein product	275	2e-73
			BAC03722.1	unnamed protein product	223	9e-58
NM_013487 NP_038515.1	Mm.4527	U:(C-D) 2.39	NP_000723.1	CD3D antigen, delta polypeptide (TiT3 complex)	228	5e-60
		,	P04234	CD3D_HUMAN T-cell surface glycoprotein CD3 delta chain precursor (T-cell receptor T3 delta chain)	228	5e-60
	:		RWHUD1	T-cell surface glycoprotein CD3 delta chain precursor	228	5e-60
	. , 1		CAA25683.1	20K T3 glycoprotein precursor	228	5e-60
			AAA51792.1	T3 antigen delta-chain	228	. 5e-60
		•	CAA27573.1	T3 delta protein	228	5e-60

			11013944	unotain dalta 112 alimo	-	6
			עדייר	ביפנים וויסוטים בייסוסים בייסו	777	2e-58
AK004773	1	U:(C-D)				
XP_125911.2	Mm.32580 2.2	2.27	NP_055686.1	KIAA0710 gene product	1150	0
	Ì		BAA31685.1	KIAA0710 protein	1150	0
			AAH24043.1	KIAA0710 gene product	1141	0
/ NM_007804		(ת ייי),11	: -			
NP_031830.1	Mm.5116	0.(C-D) 2.26	014529	CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)	1950	0
,			BAA22962.2	The human homolog of mouse Cux-2	1950	0
'			XP_027045.6	similar to Homeobox protein Cux-2 (Cut-like 2)	1949	0
		,	P39880	CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 1)	892	247
	: .		AAB26579.1	CCAAT displacement protein, CDP [luman, Peptide, 1505 aa]	892	0
			NP_001904.1	cut-like 1, CCAAT displacement protein; cut like 1, CCAAT displacement protein (Drosophila)	. 283	. 2e-75
	1	;	AAA35654.1	alternatively spliced	283	2e-75
	1		AAH25422.1	cut-like 1, CCAAT displacement protein (Drosophila)	283	2e-75
	#* **		AAG59620.1	AF271236_1 transcription factor CUX2	238	8e-62
NM_026384 NP_080660.1	Mm.1801 89	U:(C-D) 2.26	CAD38961.1	hypothetical protein	761	0
			NP_115953.2	diacylglycerol O-acyltransferase homolog 2; GS1999full	751	0
			AAH15234.1	AAH15234 Unknown (protein for MGC:17861)	751	0
			AAK84176.2	AF384161_1 diacylglycerol acyltransferase 2	751	0
			BAB40641.2	product is unknown	751	0.
			CAD13492.1	bA351K23.5 (novel protein)	340	2e-93
,			NP_477513.1	diacylglycerol O-acyltransferase 2 like 1; diacylglycerol acyltransferase 2-like	331	1e-90
			AAK84178.1	AF384163_1 diacylglycerol acyltransferase 2-like protein	331	1e-90
			AAD45832.1	AC004876_5 similar to predicted proteins AAB54240 (PID:g2088822) and S67138 (PID:g2132925)	295	1e-79
					-	

U:(C-D)	XP_088691.1 XP_088683.1	similar to bA351K23.5 (novel protein)	251	10.66
المتحدث والمتحدد المتحدد المتحدد والمتحدد المتحدد المت	_		471	
	ı	similar to bA351K23.5 (novel protein)	219	5e-57
	XP_093119.2	similar to bA351K23.5 (novel protein)	215	1e-55
	NP_079374.1	hypothetical protein FLJ22644	206	5e-53
	BAB15436.1	unnamed protein product	206	5e-53
	D) A A N/41656 1	earin. hinding protein DACH. 1	1081	-
	CAB55300.1	hypothetical protein	956	
-	CAB52564.2	d197P20.1 (novel gene)	956	
	AAN23123.1	ezrin-binding partner PACE-1	956	0
	NP 065156.4	_	954	248
	AAH14662.1	Similar to hypothetical protein LOC57147	954	0
U:(C-D) Mm.22173 2.25	D) XP_006867.4	similar to P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	286	5e-77
	Q14242	SEPL_HUMAN P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	. 286	5e-77
	A57468	P-selectin glycoprotein ligand PSGL-1 precursor, long splice form	286	5e-77
,	AAA74577.1		286	5e-77
,	NP_002997.1	selectin P ligand	. 284	2e-76
	AAC50061.1	ligand for P-selectin	284	2e-76
•	AAH29782.1	selectin P ligand	284	. 2e-76
	BAC05283.1	unnamed protein product	258	2e-68
Mm.8970 U:(C-D) 2	-D) NP_660341.2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F; similar to Phorbolin 3 (APOBECI-like)	200	
	AAH38808.1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F	199	1e-50
U:(C:D)	-		·	
28248 2.23	BAA96067.1	KIAA1543 protein	388	e-108

•	,		XP_048362.1	similar to KIAA1543 protein	388	e-108
		:	CAD38783.1	hypothetical protein	. 388	e-108
	1		AAL55764.1	AF289580_1 unknown	320	1e-87
	,		XP_036589.2	similar to KIAA1078 protein	237	2e-62
	:		AAH11385.1	Unknown (protein for IMAGE;3870900)	237	2e-62
	a parameter		BAA83030.2	KIAA1078 protein	237	2e-62
			T14744	hypothetical protein DKFZp586F0424.1	236	3e-62
2			CAB53664.1	hypothetical protein	236	3e-62
			AAH12778.1	Unknown (protein for IMAGE:3939659)	. 227	1e-59
			CAD39184.1	hypothetical protein	227	1e-59
NM_024249 NP_077211.2	Mm.3310	U:(C-D) 2.23-	NP_612637.1	hypothetical protein MGC15523	.689	0.
			AAH14642.1	AAH14642 Similar to RIKEN cDNA 1810073N04 gene	689	0
			BAC04027.1	unnamed protein product	275	1e-73
NM_030562 NP_085039.1	Mm.1832 64	U:(C-D) 2.21	BAA96008.1	KIAA1484 protein	701	0
		١.	XP_046088.1	similar to hypothetical protein MGC7599; clone MGC:7599	.029	0
			XP_085176.1	similar to hypothetical protein MGC2656	484	e-136
			NP_689660.1	hypothetical protein FLJ30803	484	e-136
			BAB70910.1	unnamed protein product	484	e-136
			BAA86560.1	KIAA1246 protein	466	e-131
			XP_166372.1	similar to hypothetical protein MGC2656	466	e-131
			NP_078785.1	hypothetical protein MGC2656	446	e-125
,			AAH03578.1	AAH03578 Unknown (protein for MGC:2656)	446	e-125
	· .		AAH25310.1	Similar to KIAA1484 protein	431	e-120
			NP_076941.2	hypothetical protein MGC3103	424	e-118
			AAH15581.2	similar to hypothetical protein MGC3103	424	e-118
	4		AAH14678.1	AAH14678 Unknown (protein for IMAGE:3860672)	274	2e-73

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NM_033614 NP_291092.1	Mm.1969 71	U:(C-D) 2.15	JC4520	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) alpha' chain	1489	0
			CAA64079.1	cone cGMP phosphodiesterase	1489	0
		; .	2207224A	cGMP phosphodiesterase	1489	0
			P51160	CNRC_HUMAN Cone cGMP-specific 3',5'-cyclic phosphodiesterase alpha'-subunit	1484	0
			AAA92886.1	cone photoreceptor cGMP-phosphodiesterase alpha' subunit	1484	0 .
		·	NP_006195.2	phosphodiesterase 6C, cGMP-specific, cone, alpha prime	1478	0
	-		AAA96392.1	phosphodiesterase A' subunit	1478	0
			NP_000274.1	phosphodiesterase 6B, cGMP-specific, rod, beta	1092	0
			P35913	CNRB_HUMAN Rod cGMP-specific 3',5'-cyclic phosphodiesterase beta-subunit (GMP-PDE beta)	1092	0
			A42828	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) beta chain	1092	250
			90.1	rod cGMP phosphodiesterase beta-subunit; PDEB	1092	0
			CAA46932.1	3',5'-cyclic-nucleotide phosphodiesterase	1092	0
,			AAH00249.1	AAH00249 phosphodiesterase 6B, cGMP-specific, rod, beta (congenital stationary night blindness 3, autosomal dominant)	1089	0
1,	ſ		CAA44569.1	cGMP phosphodiesterase beta subunit	1085	0
			B34611	3',5'-cyclic-GMP phosphodiesterase (EC 3.1.4.35) alpha chain	1075	0
	e .		NP_000431.1	phosphodiesterase 6A, alpha subunit	1074	0
	1		P16499	CNRA_HUMAN Rod cGMP-specific 3',5'-cyclic phosphodiesterase alpha-subunit (GMP-PDE alpha) (PDE V-B1)	1074	0
			AAB69155.1	cGMP phosphodiesterase	1074	0
			CAA62215.1	Rod cGMP phosphodiesterase	893	0 .
			NP_058649.2	phosphodiesterase 11A; cyclic nucleotide phosphodiesterase 11A1	409	e-113
		1	BAB16371.1	phosphodiesterase 11A	409	e-113
		,	BAB62712.1	phosphodiesterase 11A4	409	e-113
NM_007441		U:(C-D)				
NP 031467.1	Mm.10112 2.14	2.14:	NP 006483.1	aristaless-like homeobox 3	516	e-146

		٠,٠	095076	ALX3_HUMAN Homeobox protein aristaless-like 3 (Proline-rich transcription factor ALX3)	516	e-146
			AAD01418.1	homeobox protein	516	e-146
NM_017394 NP_059090.1	Mm.3556 7	U:(C-D) 2.14	NP_062823.1	solute carrier family 7, member 10; asc-type amino acid transporter 1	904	0
			Q9NS82	AAA1_HUMAN Asc-type amino acid transporter 1 (Asc-1)	904	0
		\$1. 4	BAB03213.1	asc-type amino acid transporter 1	904	0
,			AAK93960.1	AF340165_1 amino acid transporter	904	0
			CAC81900.1	ASC1 protein	904	0
			AAH35627.1	similar to solute carrier family 7	904	0
			०९०माऽ	LAT2_HUMAN Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2).	699	25
			AAF20381.1	AF171669_1 glycoprotein-associated amino acid transporter LAT2	699	0
		2	BAB21519.1	L-type amino acid transporter 2	699	0
			NP_036376.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	999	0
			CAB40137.1	SLC7A8 protein	999	0
• . .		-	AAF05695.1	AF135828_1 L amino acid transporter-2; LAT-2	534	e-151
			NP_003477.2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5; Membrane protein E16; Solute carrier family 7, member 5; 4F2 light chain	436	e-122
	.>		Q01650	LAT1_HUMAN Large neutral amino acids transporter small subunit 1 (L-type amino acid transporter 1) (4F2 light chain) (4F2 l C) (4F2 C) (CD08 light chain) (Integral	436	e-122
1		, j.		mentance protein E16) (hLAT1)		
			JG0165	LAT1 protein	436	e-122
			BAA33851.1	CD98 light chain	436	e-122
			AAD20464.1	L-type amino acid transporter subunit LAT1	436	e-122
		·	BAA84648.1	L-type amino acid transporter 1	436	e-122
			AAC61479.1	amino acid transporter B16	. 436	e-122
			AAH39692.1	Similar to solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	436	e-122

,,,,		BAA75746.1	4F2 light chain	434	e-121
Щ	മ	BAB70708.1	sodium-independent neutral amino acid transporter LAT1	434	e-121
4	741	NP_003974.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	431	e-120
I		BAA13376.1	Similar to Schistosoma mansoni amino acid permease (L25068),	431	e-120
,		AAH28216.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	. 431	e-120
1					
U:(C-D) 2.13		D59433	C. elegans protein 737093 homolog [immorted]	730	
	1	BAA13212.1	similar to C.elegans protein (Z37093)	739	
7	7	AAC03237.1	D1013901	739	0
	, , ,	XP_037574.1	similar to PTPL1-associated RhoGAP 1	739	0
	, 7,	AAN04658.1	minor histocompatibility antigen HA-1	739	252
		AAH35564.1	Similar to PTPL1-associated RhoGAP 1	739	0
		NP_004806.1	PTPL1-associated RhoGAP 1	278	2e-74
¹ī		E59430	PTPL1-associated RhoGAP protein 1 [imported]	278	2e-74
•	, ,	AAB81012.1	PTPL1-associated RhoGAP	278	2e-74
	,	NP_057657.1	Gem-interacting protein	265	2e-70
^.		D59435	Gem-interacting protein [imported]	265	2e-70
		AAF61330.1	AF132541_1 Gem-interacting protein	265	2e-70
(A)		· .			
Mm.30114 2.12		AAL14103.1	AF391100_1 alsin	1569	,0
		BAB13389.2	KIAA1563 protein	1569	0
: .		NP_065970.1	alsin	1569	0
		BAB69014.1	long form	1569	0
		NP_667340.1	hypothetical protein LOC259173	244	Se-64
		BAC04237.1	unnamed protein product	244	5e-64
i . L		BAB84944.1	FLJ00189 protein	244	9e-64

AK014599	• .					
BAB29454.1	Mm.66017	U:(C-D) 2.12	AAD43186.1	AC006029_1 Similar to Sperm Surface Protein PH-20; Similar to P38568 (PID:585674)	749	
			NP_036401.1	hyaluronoglucosaminidase 4; hyaluronidase 4	749	0
		-	AAC9883.1	hyaluronidase 4	749	0
			NP_694859.1	sperm adhesion molecule 1 isoform 2; sperm surface protein PH-20; hyaluronoglucosaminidase	385	e-106
				HYAP_HUMAN Hyaluronidase PH-20 precursor (Sperm surface protein PH-20)		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
			P38567	(Sperm adhesion molecule 1)	385	e-106
			CAA59086.1	sperm adhesion molecule gene SPAM1	385	e-106
			NP_003108.2	sperm adhesion molecule 1 isoform 1; sperm surface protein PH-20; hyaluronoglucosaminidase	385	e-106
4	·		AAH26163.1	sperm adhesion molecule 1 (PH-20 hyaluronidase, zona pellucida binding)	385	e-106
	-		AAC60607.2	PH-20	382	e-105
	:		S40465	sperm protein PH-20	382	e-105
		1	AAD24460.1	AF118821_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
			AAD53277.1	AF173154_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
	7		NP_009296.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	16-91
:	f :		NP_149349.2	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	16-91
			NP_695013.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	. 336	1e-91
		1	AAD04190.1	hyaluronoglucosaminidase 1	336	1e-91
			AAD09137.2	putative tumor suppressor	336	1e-91
			AAH35695.1	hyaluronoglucosaminidase 1	336	16-91
i	-	,	JC5584	hyalurononglucosaminidase (EC 3.2.1.35) 1 precursor	333	7e-91
NM_008969 NP_032995.1	Mm.2792	U.(C-D) 2.12	NP 000953.2	rostaglandin-endoperoxide synthase 1, isoform 1 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	1043	0
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	1043	1043	1043	1043	1043	1043	1043	1038	956	926	729	729	729	729	729	729	729	729	727	
PGH1 HUMAN Prostaglandin G/H synthase 1 precursor (Cyclooxygenase -1)	(COX-1) (Prostaglandin-endoperoxide synthase 1) (Prostaglandin H2 synthase 1) (PGH synthase 1) (PGHS-1) (PHS 1)	prostaglandin-endoperoxide synthase (EC 1.14.99.1) 1 precursor	prostaglandin endoperoxide synthase	prostaglandin endoperoxide synthase; cyclooxygenase	prostaglandin G/H synthase; PGG/HS	AF440204_1 prostaglandin-endoperoxide synthase 1	Unknown (protein for MGC:34214)	prostaglandin-endoperoxide synthase-1	prostaglandin-endoperoxide synthase 1, isoform 2 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	prostaglandin G/H synthase; PGG/HS	prostaglandin-endoperoxide synthase 2 precursor; prostaglandin G/H synthase and cyclooxygenase; cyclooxygenase-2; endoperoxide synthase type II; prostaglandin H synthase type 2; prostaglandin synthase-2; PG synthetase	PGH2_HUMAN Prostaglandin G/H synthase 2 precursor (Cyclooxygenase -2) (COX-2)(Prostaglandin-endoperoxide synthase 2) (Prostaglandin H2 synthase 2) (PGH synthase 2) (PGH synthase 2)	cyclooxygenase-2	prostaglandin endoperoxide synthase-2	PTGS2 (prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase))	AAH13734 prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	prostaglandin-endoperoxide synthase (EC 1.14.99.1) 2 precursor	cyclooxygenase-2	endoperoxide synthase type Π	
	P23219	JH0259	AAA03630.1	AAB21215.1	AAB22217.1	AAL33601.1	AAH29840.1	AAA36439.1	NP_542158.1	AAB22216.1	NP_000954.1	P35354	AAA57317.1	BAA05698.1	CAB41240.1	AAH13734.1	A46150	AAA58433.1	AAA35803.1	
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NM_010225 NP_034355.1	Mm.6260	U:(C-D) 2.11		NP_001443.1 forkhead box F2; forkhead (Drosophila)-like 6	521	e-147
			Q12947	FXF2_HUMAN Forkhead box protein F2 (Forkhead-related protein FKHL6) (Forkhead-related transcription factor 2) (FREAC-2) (Forkhead-related activator-2)	521	e-147
			T09474	forkhead protein FREAC-2	521	P-147
-			AAC32226.1	forkhead protein FREAC-2	52.1	P-147
	-	-	AAD19875.1	forkhead transcription factor	521	e-147
	:		2208384B	transcription factor FREAC-2	508	e-143
	i.		NP_001442.1	forkhead box F1; forkhead (Drosophila)-like 5; Forkhead, drosophila, homolog-like 5; forkhead-related activator 1 Flomo		3e-66
				sapiens]		- ,
			Q12946	FXF1_HUMAN Forkhead box protein F1 (Forkhead-related protein FKHL5) (Forkhead-related transcription factor 1) (FREAC-1) (Forkhead-related activator-1)	251	3e-66
*	ŧ	·	AAC50399.1	FREAC-1	25.1	39 66
	•		AAC61576.1	forkhead transcription factor	25.1	00-00
		:	2208384A	transcription factor FREAC-1	251	36-00
NM_028770 NP_083046.1	Mm.3338 5	U.(C-D) 2.1	XP_096612.2	similar to RIKEN cDNA 1200016G03	561	e-159
; ; ;			CAB76832.1	cytokeratin	0.70	65.70
3	The second secon		NP_004684.1	cytokeratin type II	270	10 71
			CAA76730.1	cytokeratin type II	270	1e-71
			AAH24292.1	keratin 5 (epidernolysis bullosa simplex, Dowling-Meara/Kobner/Weber-Cockayne types)	261	56-69
			AAA36145.1	keratin K5	2,60	70 60
			NP_000415.1	keratin 5; Keratin-5; 58 kda cytokeratin; keratin, type II cytoskeletal 5; cytokeratin 5	092	76-69
			P13647	K2C5_HUMAN Keratin, type II cytoskeletal 5 (Cytokeratin 5) (K5) (CK 5) (58 kDa cytokeratin)	260	76-69
			A29904	keratin 5, type II, epidermal	260	70.60
			AAA36143.1	keratin type II	260	70-07
· ·			AAF97931.1	AF274874_1 keratin 5	260	70-60

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	1e-68	1e-68	1e-68	1e-68	1e-68	1e-68	1e-68	e-167	e-167	e-167	e-167	e-167	e-167	e-166	e-166	e-166	e-127	e-127	e-127	e-127	e-177	e-127	e-127	e-125	e-121	e-109	e-109
	259	259	259	259	259	259	259	585	585	585	585	585	585	583	583	583	451	451	451	451	451	451	451	445	432	392	392
		1 Keratin 8	1 human cytokeratin 8	1 AAH00654 keratin 8	keratin 8, type II cytoskeletal	K2C8_HUMAN Keratin, type II cytoskeletal 8 (Cytokeratin 8) (K8) (CK 8)	1 cytokeratin 8	2 uncoupling protein 2	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP 2) (UCPH)		uncoupling protein 2	uncoupling protein-2	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)		uncoupling protein 2	uncoupling protein-2	1 uncoupling protein 3, isoform UCP3L	UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)	uncoupling protein UCP3, mitochondrial	UCP3	uncoupling protein 3	uncoupling protein-3	AF050113_1 uncoupling protein-3	uncoupling protein 3	uncoupling protein 3	uncoupling protein 3, isoform UCP3S	UCP3S
	NP_002264.1	CAA52882.1	AAB18966.1	AAH00654.1	A34720	P05787	AAA35763,1	D) NP_003346.2	P55851	AAC51336.1	AAC39690.1	AAD21151.1	AAH11737.1	AAB53091.1	CAA11402.1	AAB48411.1	NP_003347.1	P55916	JC5522	AAC51367.1	AAC51369.1	AAC51767.1	AAG02284.1	AAC18822.1	AAC51785.1	NP_073714.1	AAC51356.1
						_		U:(C-D) 2.09							, V.,					·		,		·			
							÷ .	Mm.1444 13	:	1.	,		·		.'·	,					,	* **					
								NM_011671 NP_035801.1	1									÷							:		

			1			
			NP_068605.1	J68605.1 uncoupling protein 1; mitochondrial brown fat uncoupling protein	353	. 2e-97
	!s :		G01858	uncoupling protein 1, mitochondrial	353	2e-97
		1	AAA85271.1	uncoupling protein	353	2e-97
			P25874	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	350	2e-96
	-		CAA36214.1	uncoupling protein	250	2e-96
			AAH08392.1	AAH08392 Similar to uncoupling protein 3 (mitochondrial, proton carrier)	206	5e-53
NM_011933 NP_036063.1	Mm.3576 0	U:(C-D) 2.09	NP_065715.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
	. : . :		CAB92744.1	c359F1.1 (novel protein (ortholog of mouse and rat peroxisomal 2,4-dienoyl-coA reductase (PDCR, DCR-AKL)))	466	e-131
			CAC05664.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
			AAK61231.1	AE006463_11 2-4-dienoyl-Coenzyme A reductase 2 peroxisomal like	466	e-131
	,	~	AAH10740.1	AAH10740 2,4-dienoyl CoA reductase 2, peroxisomal	797	e-131
			AAH11968.1	AAH11968 Similar to 2,4-dienoyl CoA reductase 2, peroxisomal	370	e-105
NM_019424 NP_062297.1	Mm.1948 06	U:(C-D) 2.08	AAL50684.1	AF450133_1 Hermansky-Pudlak syndrome	1065	0
			NP_000186.1	Hermansky-Pudlak syndrome protein; Hermansky-Pudlak syndrome gene; Hermansky-Pudlak syndrome	1064	0
,	à	-	092902	HPS1_HUMAN Hermansky-Pudlak syndrome 1 protein	1064	0
		• .	AAB17869.1	Hermansky-Pudlak syndrome protein	1064	0
			AAB70662.1	Hermansky-Pudlak syndrome protein	866	0
			AAH00175.1	AAH00175 Hermansky-Pudlak syndrome	411	e-114
			AAC52074.1	alternative Hermansky-Pudlak syndrome associated protein	409	e-114
	. ,		1			
NM_008433	:			-		
NP_032459.1	Mm.9911	U:(C-D) 2.06	NP_002241.1	intermediate conductance calcium-activated potassium channel protein 1; putative erythrocyte intermediate conductance calcium-activated potassium Gardos channel	209	e-173
			015554	KCN4_HUMAN Intermediate conductance calcium-activated potassium channel protein 4 (SK4) (KCa4) (IK1) (IKCa1) (Putative Gardos channel)	607	e-173

7	.		AAB82739.1	calcium-activated potassium channel	209	e-173
			AAC36804.1	intermediate conductance calcium-activated potassium channel	607	e-173
-1			AAC23541.1	hIK1	607	e-173
,			AAC51913.1	intermediate conductance calcium-activated potassium channel	607	e-173
		:	AAG26917.1	intermediate-conductance calcium-activated potassium channel 1	. 607	e-173
, 1			AAH15337.1	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	209	e-173
			AAK81862.1	AF395661_1 potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	909	e-173
3			AAL10706.1	small-conductance calcium-activated potassium channel SK3	286	5e-77
		,	NP 002240.2	small conductance calcium-activated potassium channel protein 3 isoform a	285	16-76
			O9UGI6	KCN3_HUMAN Small conductance calcium-activated potassium channel protein 3 (SK3) (SKCa3)	285	1e-76
***			CAB61331.1	SK3 protein	285	1e-76
			AAK15345.1	AF336797_1 small-conductance calcium-activated potassium channel	285	1e-76
			T09172	probable calcium-activated potassium channel KCNN3	282	1e-75
			AAC26099.1	calcium-activated potassium channel	282	1e-75
	· i		092952	KCN1_HUMAN Small conductance calcium-activated potassium channel protein 1 (SK1)	278	2e-75
	. 3		AAB09562.1	small-conductance, calcium-activated potassium channel SK1	278	2e-75
			AAD37507.1	small-conductance calcium-activated potassium channel 1	278	2e-75
			NP 002239.2	small conductance calcium-activated potassium channel protein 1	278	2e-75
	2		AAK84039.1	AF397175_1 small-conductance calcium-activated potassium channel	280	5e-75
			Q9H2S1	KCN2_HUMAN Small conductance calcium-activated potassium channel protein 2 (SK2)	279	7e-75
			AAG16728.1	AF239613_1 apamin-sensitive small-conductance Ca2+-activated potassium channel	279	7e-75
			NP 067627.2	small conductance calcium-activated potassium channel protein 2 isoform a; apamini-sensitive small-conductance Ca2+-activated potassium channel	7.79	7e-75

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NM_013486 NP_038514.1	Mm.2284	U:(C-D) 2.06	RWHUC2	T-cell surface glycoprotein CD2 precursor	255	1e-67
		-	AAA35571.1	T-cell surface antigen CD2 precursor	255	1e-67
			AAA53095.1	T11 surface antigen	255	1e-67
			CAC14840.1	dJ655N15.1 (CD2 antigen (p50), sheep red blood cell receptor)	255	1e-67
			AAA51946.1	CD2 surface antigen	255	1e-67
			NP 001758.1	CD2 antigen (p50), sheep red blood cell receptor; lymphocyte-function antigen-2	252	8e-67
	-		P06729	CD2_HUMAN T-cell surface antigen CD2 precursor (T-cell surface antigen T11/Leu-5) (LFA-2) (LFA-3 receptor) (Erythrocyte receptor) (Rosette receptor)	252	8e-67
			AAA51738.1	surface antigen CD2 precursor	252	8e-67
			CAA30721.1	T-cell surface antigen	. 252	8e-67
	:		AAH33583.1	CD2 antigen (p50), sheep red blood cell receptor	252	8e-67
NM_029796 NP_084072.1	Mm.1769 46	U:(C-D) 2.06	NP_443204.1	leucine-rich alpha-2-glycoprotein	330	3e-90
		•	P02750	A2GL_HUMAN Leucine-rich alpha-2-glycoprotein precursor (LRG)	330	3e-90
			AAK95527.1	AF403428_1 leucine-rich alpha-2-glycoprotein	330	3e-90
			NBHUA2	leucine-rich alpha-2-glycoprotein	329	06-99
			AAH34389.1	leucine-rich alpha-2-glycoprotein	327	2e-89
X71479 CAA50585.1	NULL	U:(C-D) 2.06	CAA50586.1	cytochrome P450	268	2e-72
			NP_000769.1	cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega; alkane-1 monooxygenase; lauric acid omega-hydroxylase	267	4e-72
			153015	fatty acid omega-hydroxylase (EC 1.14.15) cytochrome P450 4A11	267	4e-72
			AAB29502.1	fatty acid omega-hydroxylase; CYP4A11	267	4e-72
			165981	fatty acid omega-hydroxylase (EC 1.14.15) cytochrome P450 4A11	267	4e-72
		-	AAB29503.1	fatty acid omega-hydroxylase; CYP4A11v	267	4e-72
			Q02928	CP4Y_HUMAN Cytochrome P450 4A11 precursor (CYPIVA11) (Fatty acid omega-hydroxylase) (P-450 HK omega) (Lauric acid omega-hydroxylase) (CYP4AII) (P450-HI-0Mega)	265	2e-71
				(-0-)		

,			JX0331	laurate omega-hydroxylase (EC 1.14.15.3) cytochrome P450 4A11 (HL24)	265	2e-71
			AAA58436.1	cytochrome P450	265	2e-71
			05491.1	fatty acids omega-hydroxylase (cytochrome P450HL omega)	265	2e-71
			1908216A	fatty acid omega-hydroxylase (cytochrome P450 4A)	265	2e-71
			BAA02864.1	fatty acid omega-hydroxylase	265	2e-71
			76722.1	AF208532_1 fatty acid omega-hydroxylase CYP4A11	261	2e-70
			CAB72105.1	dJ18D14.4 (cytochrome P450, subfamily IVA, polypeptide 11)	253	. 66-68
1				Unknown (protein for MGC:40051)	202	1e-52
				unnamed protein product	202	1e-52
			BAC03751.1	unnamed protein product	202	1e-52
		U:(C-D)	014753	OVO1_HUMAN Putative transcription factor Ovo-like 1 (hOvo1)	468	e-131
NM_019935 N NP_064319.1 3	Mm.3832 3	2.05 U:(IR-D) 2.41	· · · · · · · · · · · · · · · · · · ·			
			NP_004552.1	OVO-like 1 binding protein; putative transcription factor OVO-like 1; ovo (Drosophila) homolog-like 1	367	e-101
	_		AAB72084.1	OVO-like 1 binding protein	367	e-101
		7	NP_067043.1	zinc finger protein 339; ovo-like 2 (Drosophila)	275	3e-73
			BAB14002.1	unnamed protein product	275	3e-73
:			Q9BRP0	Z339 HUMAN Zinc finger protein 339	271	2e-72
1:			AAH06148.1	AAH06148 putative zinc finger protein from EUROIMAGE 566589	271	2e-72
		:	CAB45151.1	hypothetical protein, similar to (AF134804) putative zinc finger transcription factor OVO1 [Mus musculus]	. 238	3e-62
NM_012006 NP_036136.1	Mm.1978	U:(C-D) 2.05	XP_170752.1	similar to peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	602	e-172
			P49753	PTE2_HUMAN Peroxisonal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	009	e-171
			JC7367	second peroxisomal thioesterase	009	e-171
		1.	AAF97985.1	peroxisomal long-chain acyl-coA thioesterase	009	e-171

			1			
	,		AAH04436.1	AAH04436 Unknown (protein for MGC:3983)	909	e-171
			AAH06500.1	AAH06500 Unknown (protein for MGC:2366)	009	e-171
			NP_006812.2	peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	599	e-171
			AAH06335.1	AAH06335 peroxisomal long-chain acyl-coA thioesterase	599	e-171
	4		BAA91989.1	unnamed protein product	598	e-171
			NP_689544.1	hypothetical protein FLJ31235	494	e-139
,			BAC04313.1	umamed protein product	494	e-139
			AAC42007.1	ORF; putative	405	e-113
			XP_090885.1	similar to Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	280	4e-75
		,	NP_001692.1	bile acid Coenzyme A: amino acid N-acyltransferase; glycine N-choloyltransferase	265	2e-70
			A53965	bile acid-CoA amino acid N-acyltransferase	265	2e-70
i i			AAC37550,1	bile acid CoA: Amino acid N-acyltransferase	265	2e-70
			AAH09567.1	AAH09567 bile acid Coenzyme A: amino acid N-acyltransferase (glycine N-choloyltransferase)	265	2e-70
AK004963		(U-C-D)				
BAB23703.1	Mm.186	2.04	NP_055419.1	Tax interaction protein 1	243	4e-64
in the second			AAB84248.2	Tax interaction protein 1	243	4e-64
4.5		,	AAG44368.1	AF234997_1 glutaminase-interacting protein 3	243	4e-64
			AAK69111.1	AF277318_1 tax-interacting protein 1	243	4e-64
	ì		AAH23980.1	Tax interaction protein 1	243	4e-64
			AAF43104.1	TIP1	228	2e-59
AK008849	: .					
BAB25928.ī	U:(C Mm.45435 2.04	U:(C-D) 2.04	NP_079119.2	duodenal cytochrome b; hypothetical protein FLJ23462	391	e-109
			CAB66628.1	hypothetical protein	391	e-109
. ,			BAB15661.1	unnamed protein product	386	e-107

	,			eimilar to data course. CDTTD course from 0011000		
			XP_166224.2	HYPOTHETICAL 31.6 KDA PROTEIN~putative	196	6e-50
			NP_705839.1	hypothetical protein MGC20446	196	6e-50
	-		BAC11698.1	unnamed protein product	196	6e-50
NM_008532 NP_032558.1	Mm 4259	U:(C-D) 2.03	P16422	TTD1_HUMAN Tumor-associated calcium signal transducer 1 precursor (Major gastrointestinal tumor-associated protein GA733-2) (Epithelial cell surface antigen) (Epithelial glycoprotein) (EGP) (Adenocarcinoma-associated antigen) (KSA) (KS 1/4 antigen) (Cell surface altographic Tenes 1)		
	-		CAA32870.1	KSA preproantigen pentide	440	e-125
	a.		AAA36151.1	adenocarcinoma-associated antigen precursor (KSA)	446	e-125
		<i>:</i>	AAA59543.1	KS1/4 antigen	446	e-125
			NP 002345.1	tumor-associated calcium signal transducer 1 precursor; membrane component, chromosome 4, surface marker (35kD glycoprotein); MK-1 antigen; antigen identified by monoclonal antibody AUA1	446	. e 175
ŧ			B48149	epithelial glycoprotein antigen GA733-2 precurso	446	e-125
			AAA35861.1	carcinoma-associated antigen GA733-2	446	ė-125
			AAB00775.1	carcinoma-associated antigen GA733-2	446	e-125
-	* /		AAH14785.1	tumor-associated calcium signal transducer 1	446	e-125
			23.1	epithelial glycoprotein (EGP) precursor	444	e-124
	· .		A48149	carcinoma-associated antigen GA733-1 precursor	265	2e-70
*		1	CAA31781.1	GA733-1 protein (AA 1-323)	265	2e-70
			CAA54801.1	gp50/TROP-2	265	2e-70
			AAH09409.1	Unknown (protein for MGC:10655)	265	2e-70
		***************************************	NP_002344.1	tumor-associated calcium signal transducer 2 precursor; membrane component, chromosome 1, surface marker 1 (40kD glycoprotein, identified by monoclonal antibody GA733); epithelial glycoprotein-1	263	0E-70
		,	CAA54799,1	gp50/Trop-2	263	6e-70
			P09758	TID2_HUMAN Tumor-associated calcium signal transducer 2 precursor (Pancreatic carcinoma marker protein GA733-1) (Cell surface glycoprotein Trop-2)	262	1e-69
			AAA52505.1	\(\sum_{\text{A52505.1}} \) GA733-1 protein precursor	262	1e-69

NIM DOOTED					-	
00 / 00 Turk		U:(C-D)				
NP 033910.1	Mm.16106 2.02	2.02	P01028	CO4_HUMAN Complement C4 precursor [Contains: C4A anaphylatoxin]	2587	0
			CAHU	complement C4A precursor [validated]	2586	0
		÷	AAA51855.1	complement component C4A	2586	0
		:	NP_009224.1	complement component 4A preproprotein; acidic C4; Rodgers form of C4; complement component 4S	2583	C
	1		CAB89302.	dJ34F7.4 (complement component 4A)	2582	
			NP_000583.1	complement component 4B preproprotein; Chido form of C4; basic C4; complement component 4F	2581	C
-			AAB67980.1	complement component C4	2581	0
		1. 2.	AAB59537.1	complement component C4A	2563	0
1			AAA99717.1	complement C4B precursor	2465	0
,			NP_000055.1	complement component 3 precursor	624	e-178
		.:	P01024	CO3_HUMAN Complement C3 precursor	624	e-178
			C3HO	complement C3 precursor [validated]	624	e-178
		,	AAA85332,1	complement component G3	624	e-178
	- 1		AAA59651.1	complement component C4B	573	e-163
	:		1HZF	A Chain A, C4adg Fragment Of Human Complement Factor C4a	544	e-154
NM_008874						
NP_032900.1	Mm.6888	U:(C-D) 2	NP 000923.1	phospholipase C, beta 3 (phosphatidylinositol-specific)	2015	C
				PIP3 HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta 3	2012	2
				(LTC-0ca-2) (Thosphonpase C-0eta-3)	2015	0
			682 1	phosphoripase C-Octa-3	2015	0
			1,00	puospuonpase C-pera-3	2015	0
				phospholipase C beta 3	1967	0
			485776.1	phospholipase C beta 3	1967	0
			AAH32659.1	Similar to phospholipase C, beta 3	1824	0

			607000	the state of the s	-	
				phosphotipase $C(EC 3.1.4.3)$, phosphatidylinositol-specific	1663	0
		:	CAA78903.1	phospholipase c	1663	c
	*		NP 056007 1	phospholipase C, beta 1 (phosphoinositide-specific); phosphoinositide-specific phospholipase C-beta 1; phospholipase C beta 1; phospholipase C, beta 1 (phosphoinositide-specific)		2
			11	· (Parosparancespectate)	1197	0
			99ON6O	PIBI_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta (PLC-beta-1) (Phospholipase C-beta-1) (PLC-1) (PLC-154)	1197	C
		2 2	CAB98142.1	phospholipase C-beta-1a	1197	;
			CAB98143.1	phospholipase C-beta-1b	1192	0
			AAF86613.1	phospholipase C beta 1	1154	0
	: (BAA25507.	KIAA0581 protein	1047	0
			NP 004564.1	phospholipase C, beta 2	934	0
			Q00722	PIB2_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta 2 (PLC-beta-2) (Phospholipase C-beta-2)	934	C
			A43346	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase (EC 3.1.4.11) beta-2	934	0
:			AAA36453.1	phospholipase C-beta-2	934	0
			T46339	hypothetical protein DKFZp434A0814.1	885	0
	·		CAB70666.1	hypothetical protein	885	0
NM_010129 NP_034259.1	Mm.2082 9	U:(C-D) 2	NP_001416.1	epithelial membrane protein 3	250	1e-66
			P54852	EMP3_HUMAN Epithelial membrane protein-3 (EMP-3) (VMP protein) (Hematopoietic neural membrane protein) (HNMP-1)	250	1e-66
	ì	•	AAC50920.1	YMP	250	1e-66
			AAC51730.1	hematopoietic neural membrane protein	250	1e-66
			AAH09718.1	AAH09718 epithelial membrane protein 3	.250	1e-66
			JC5045	epithelial membrane protein 3	244	6e-65
:.			CAA64394.1	epithelial membrane protein-3	244	6e-65
NM_011644 NP_035774.1	Mm.8361 5	U:(C-D) 2	NP_004612.2	transient receptor potential cation channel, subfamily C, member 6; transient receptor potential channel 6	427	e-119

			Q9Y210	TRP6 HUMAN Short transient receptor notential channel 6 (TmC6)	TCV.	110
			CAA06943.1	transient receptor potential protein	174	6-119
;			A A C 63289 2	tanciant recentor notartial acotain C	174	6-119
			CAC01684 1	terminate receptor potential protein 0	427	e-119
				nausicut teceptoi potentiai channei o	427	e-119
			NP_003296.1	transient receptor potential cation channel, subfamily C, member 3; transient receptor potential channel 3	421	e-117
			Q13507	TRP3_HUMAN Short transient receptor potential channel 3 (TrpC3) (Htrp-3) (Htrp3)	421	e-117
			CAA74083.1	transient receptor potential related channel 3 protein	421	e-117
-	·		AAC51653.1	calcium influx channel	421	e-117
			NP_065122.1	putative capacitative calcium channel	411	e-114
			О9НСХ4	TRP7_HUMAN Short transient receptor potential channel 7 (TrpC7) (TRP7 protein)	441	e-114
			CAC03489.1	putative capacitative calcium channel	411	e-114
ì			CAD19069.1	short transient receptor potential channel 7	409	e-113
			AAF22928.1	AF063823_1 trp-related protein 4 truncated variant beta	369	e-101
			AAL24550.1	AF421359_1 transient receptor potential channel 4 beta splice variant	369	e-101
: '		·	AAL24551.1	AF421360_1 transient receptor potential channel 4 epsilon splice variant	369	e-101
		į	NP_057263.1	transient receptor potential 4; transient receptor potential channel 4	369	e-101
			Q9UBN4	TRP4_HUMAN Short transient receptor potential channel 4 (TrpC4) (trp-related protein 4) (hTrp-4) (hTrp-4)	369	e-101
:		;	AAD51736.1	AF175406_1 transient receptor potential 4	. 369	e-101
			AAF22927.1	AF063822_1 trp-related protein 4	369	e-101
		-	AAL24549,1	AF421358_1 transient receptor potential channel 4 alpha splice variant	360	P.10
	i		AAF22929.1	AF063824_1 trp-related protein 4 truncated variant delta	369	e-101
			NP_036603.1	transient receptor potential cation channel, subfamily C, member 5; transient receptor potential channel 5	359	2e-98
			Q9UL.62	TRP5_HUMAN Short transient receptor potential channel 5 (TrpC5) (Htrp-5) (Htrp5)	359	2e-98
			AAF00002.1	AF054568_1 transient receptor potential calcium channel 5	359	2e-98
			CAC01686.1	transient receptor potential channel 6, variant delta377-431	333	1e-90

Subtable 1C: Mixed Genes and Proteins

E-value							180	176	9,9	3.59	3-59	3-52		,						171	171	164			164	
Score	(bits)	1004.0	,	1004 0	1003	632 0	630 e-180	615 e-176	230 8F-60	228 2E-59	228 2E-59	204 6E-52	712 0	·	•	712 0	7110	710 0	707	600 e-171	600 -171	577 e-164	· ·	••	577 e-164	<u>· </u>
Human Protein Name		likely ortholog of mouse Shc SH2-domain binding protein 1; hypothetical protein FLJ22009		Unknown (protein for MGC:26900)	unnamed protein product.		unnamed protein product	AAH00960 Unknown (protein for IMAGE:3451160)	GE36	chromosome 1 open reading frame 14; GE36 gene	AF288398_1 C1orf14	AF288397 1 Clorf14	DPG2_HUMAN DNA polymerase gamma subunit 2, mitochondrial precursor	(varioculoration Diver polymerase accessory subunit) (Fold-beta) (MIFOLB) (DNA polymerase gamma accessory 55 kDa subunit) (p55)		AF142992_1 DNA polymerase gamma accessory subunit	AF177201_1 mitochondrial DNA polymerase accessory subunit precursor	AAH09194 Unknown (protein for MGC:15231)	AF184344 1 DNA polymerase accessory subunit precursor		mitochondrial DNA polymerase accessory subunit precursor	cell division cycle 2 protein, isoform 1; cell division control protein 2 homolog;	cyclm-dependent kinase 1; p>4 protein kinase; cell cycle controller CDC2		CDC2_HUMAN Cell division control protein 2 homolog (p34 protein kinase)	(Cyclin-dependent kinase 1) (CDK1)
Human	Proteins	NP_079021.2		AAH30699.1	BAB71049.1	XP_015700.2	BAB15208.1	AAH00960.1	AAG45336.1	NP_112195.1	AAG60617.1	AAG60616.1	Q9UHN1			AAD50382.1	AAD56640.1	AAH09194.1	AAD56542.1	NP_009146.1	AAC51321.1	 NP_001777.1			P06493	·
Behavior		U:(C-IR) 2.88 F.(75 E)	F:(IK-D) -2.63		. 3 1.			,		1			U:(C-IR)	F:(IR-D)	-3.23			·				U:(C-IR)	F:(TR-D)	-2.86	,	
Unigene		Mm.37801				; ·							Mm.859									Mm.4761				
Mouse Gene	riotem	NM_011369 NP_035499.1				,	,	3	77. 4.				NM_015810 NP_056625.1									659L00_MN	NP 031685.1		444	

					:	
			A29539	protein kinase (EC 2.7.1.37) cdc2	577	577 e-164
			CAA28963.1	CDC2 polypeptide (CDC2) (AA 1-297)	577	e-164
			CAA68376.1		_	e-164
			AAH14563.1	Similar to cell division cycle 2, G1 to S and G2 to M	577	577 e-164
·			AAM34793.1		577	577 e-164
	,		1306392A		5777	577 e-164
1			NP_203698.1		409	409 e-114
			BAA26001.1		400	409 6-114
			NP_001249.1	cyclin-dependent kinase 3	393	393 e-109
,			Q00526	CDK3_HUMAN Cell division protein kinase 3	393	393 e-109
			S23382	protein kinase (EC 2.7.1.37) cdk	393	393 e-109
	-		CAA47001.1	serine/threonine protein kinase [Homo sapiens]	393	e-109
		-	CAA43807.1		390	e-108
			NP_001789.2	cyclin-dependent kinase 2, isoform 1; cdc2-related protein kinase; cell devision kinase 2; p33 protein kinase	389	e-108
			P24941	CDK2_HUMAN Cell division protein kinase 2 (p33 protein kinase)	389	389 e-108
			A41227	protein kinase (EC 2.7.1.37) cdk2	389	389 e-108
			1KE5	A Chain A, Cdk2 Complexed With N-Methyl-4-{[(2-0xo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}benzenesulfonamide	389	389 e-108
}.	:		1KE6	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With N-Methyl-{4-[2-(7-Oxo-6,7-Dihydro-8h-[1,3]thiazolo[5,4-E]indol-8-Ylidene)hydrazino]phenyl} methanesulfonamide	1	389 e-108
2			1KE7	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-{[(2,2-Dioxido-1, 3-Dihydro-2-Benzothien-5-Yl)amino]methylene}-5-(1,3-Oxazol-5-Yl)-1,3-Dihydro-2h-Indol-2-One	389	3 <u>8</u> 9 e-108
		:	1KE8	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 4-{[(2-Oxo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}-N-(1,3-Thiazol-2-Yl)benzenesulfonamide	389	389 e-108
	- 1		1KE9	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-{[4-({[arnino(Imino)methyl]aminosulfonyl)anilino]methylene}-2-0xo-2,3-Dihydro-1h-Indole	389	e-108
			1FIN	A Chain A, Cyclin A - Cyclin-Dependent Kinase 2 Complex	389	e-108
			IFIN	C Chain C, Cyclin A - Cyclin-Dependent Kinase 2 Complex	389	389 e-108

389 e-108	389 e-108	389 - 108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	-389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108
C Chain C, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	A Chain A, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	Human Cyclin-Dependent Kinase 2	Human Cyclin-Dependent Kinase 2	A Chain A, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	A Chain A, Crystal Structure Of The Human Cdk2 Kinase Complex With Cell Cycle-Regulatory Protein Ckshs1	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4- [(6-Amino-4-Pyrimidinyl) Amino]benzenesulfonamide	P Chain P, Crystal Structure Of Human Cdk2 (Unphosphorylated) In Complex With Pkt049-365	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4-[3-Hydroxyanilino]-6,7-Dimethoxyquinazoline	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With An Oxindole Inhibitor.	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Purvalanol B	Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Staurosporine	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Cdk4 Inhibitor	A Chain A, Crystal Structure Of Human Cyclin Dependent Kinase 2 (Cdk2) In Complex With The Inhibitor H717	A Chain A, Human Cyclin-Dependent Kinase 2 Complexed With The Inhibitor Hymenialdisine	C Chain C, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	cdc2-related protein kinase			cyclin A dependent p33 kinase:SUBUNIT=2
IFVV	1FVV	1HCL	1HCK	1F5Q	IBUH	1JSV	1JVP	1DI8	1FVT	1CKP	14Q1	1GIH	1G5S	1DM2	1F5Q	AAA35667.1	AAH03065.1	AAM34794.1	1717387A
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		,					1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1								V al				
	1											1.				1			

	÷	IEIX	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu6027	389	389 e-108
	:	1EIV	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu2058	389	e-108
		1B38	A Chain A, Hunan Cyclin-Dependent Kinase 2	389	389 e-108
		1B39	A Chain A, Human Cyclin-Dependent Kinase 2 Phosphorylated On Thr 160	389	e-108
		1E9H	C Chain C, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	387	e-107
	:	1E9H	A Chain A, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	387	e-107
•	:	1H1P	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	387	e-107
		IHIP	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	. 387	e-107
F		1H1Q	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	387	387 e-107
		1H1Q	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	387	387 e-107
	1 () () () () () () () () () (1H1R	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	387	387 e-107
		1H1R	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	387	387 e-107
		1H1S	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	387	387 e-107
		1H1S	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	387	387 e-107
		1GY3	A Chain A, Pedk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	387	e-107
		1GY3	C Chain C, Pedk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	387	e-107
		1QMZ	A Chain A, Phosphorylated Cdk2-Cyclyin A-Substrate Peptide Complex	387	387 e-107
		1QMZ	C Chain C, Phosphorylated Cdk2-Cyclyin A-Substrate Peptide Complex	387	387 e-107
		Т	cdk2	387	e-107
NM_00/418	Mm.57205 U:(C-IR)	F18825	A2AC_HUMAN Alpha-2C-adrenergic receptor (Alpha-2C adrenoceptor) (Subtype C4)	929	0
				_	_

	626 0.	020 0	634 0	601 6 171	601 0-171	601 6-171	601 6-171	385 -106	385 6-106	384 e-106	384 e-106	201 - 100	384 e-100	384 6-106	384 P. 106	382 e-105	381 e-105	358 7F-98	355 2E-97		355 2E-97	258 4E-68	258 4E-68	258 4E-68	764 0	·			764 0
	AF280399 1 alpha 2C adrenergic recentor	alpha2CII-adrenergic receptor	AF280400 1 alpha 2C adrenergic receptor variant	alpha-2C-adrenergic receptor; alpha2-AR-C4	alpha-2C-adrenergic receptor	kidney alpha-2-adrenergic receptor	alpha2-C4-adrenergic receptor	alpha-2A-adrenergic receptor	alpha-2 adrenergic receptor old gene name 'ADRA2R'	alpha-2A-adrenergic receptor; platelet type adrenoceptor, alpha-2A; alpha-2A adrenoceptor; alpha-2AAR subtype C10	A2AA_HUMAN Alpha-2A adrenergic receptor (Alpha-2A adrenoceptor) (Alpha-2AAR subtype C10)	AF281308 1 alpha 2A adrenergic recentor	adrenergic receptor alpha-2A	_						olyhood odrawania maanta.	other D education months of 1-1-2	apua 20-aucust gio receptor, apua-2-aurenergic receptor-like 1	alpha-zn-amenergic receptor	alpha-2-adrenergic receptor (alpha-2 C2) old gene name 'ADRA2RL1'	actin, alpha, cardiac muscle precursor		1		similar to actin, alpha, cardiac
	AAG28076.1	BAA02737.1	AAG28077.1	NP 000674.1	A31237	AAA35513.1	AAC78723.1	A34169	AAA51665.1	NP_000672.2	P08913	AAF91441.1	AAG00447.2	AAK26743.1	AAK51162.1	AAK01634.1	AAA51664.1	AAK01635.1	P18089	A A B62558 1	NP 000673 1	A 37773	7777	A51666.1	NF_005150.1				XP 012405.3
F:(IR-D) -2.1									·		.:			·					,	. :				-	0:(C-IK)	F:(C-D) -	2.42	F:(JK-D) -5.6	
•									,	;	'-	-			·							,		707	MIII.080	:'	· .:		; >
NP_031444.1													-					,						T	ODO COO TAINT	NP_033738.1			

200	J5/U	U 8 2	239	8 									2	72									1	· C	I/U	152	UUZ	5/00	133	90			
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	ACTC HUMAN Actin, alpha cardiac	actin, cardiac muscle	alpha-cardiac actin	AAH09978 actin, alpha, cardiac muscle		_	ACTS HUMAN Actin, alpha skeletal muscle (Alpha-actin 1)	actin alpha 1, skeletal muscle	alpha-actin	alpha-skeletal actin precursor	AF182035 1 skeletal muscle alpha-actin precursor	Similar to actin, alpha 1, skeletal muscle	alpha 2 actin; alpha-cardiac actin			AAH17554 actin, alpha 2, smooth muscle, aorta	actin alpha 2, aortic smooth muscle	alpha-actin	actin, gamma 2 propeptide; actin, alpha-3	ACTH_HUMAN Actin, gamma-enteric smooth muscle (Alpha-actin 3)	actin gamma, enteric smooth muscle	gamma-actin (AA 1-376)	enteric smooth muscle gamma-actin	Similar to actin, gamma 2, smooth muscle, enteric		actin, gamma 1 propeptide; cytoskeletal gamma-actin; actin, cytoplasmic 2	ACTG_HUMAN Actin, cytoplasmic 2 (Gamma-actin)	actin gamma 1	gamma-actin	gamma-actin	actin, gamma 1		actin, gamma 1
	P04270	ATHUC	AAB59619.1	AAH09978.1	NP 001091.1	XP_001869.1	P02568	ATHU	AAB59376.1	AAA60296.1	AAF02694.1	AAH12597.1	NP 001604.1	P03996	CAA32064.1	AAH17554.1	ATHUSM	AAA51577.1	NP_001606.1	P12718	A40261:	CAA34814.1	BAA00546.1	AAH12617.1	JC5818	NP 001605.1	P02571	ATHUG	CAA27723.1	AAA51579.1	AAH00292.1	AAH01920.1	AAH07442.1
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actin, gamma 1	Similar to actin, gamma 1	Similar to actin, gamma 1	actin, gamma 1	actin, gamma 1	actin, gamma 1	actin, gamma 1	beta actin; beta cytoskeletal actin	ACTB HUMAN Actin, cytoplasmic 1 (Beta-actin)	actin beta	beta-actin	cytoplasmic beta actin	actin, beta	actin, beta	actin, beta	actin, beta	actin, beta	actin, beta	actin, beta	mutant beta-actin (beta'-actin)	chromosome 21 open reading frame 33; human HES1 protein, homolog to E.coli and	zeoransn eð í protein	w i i i i i i i i i i i i i i i i i i i	(GT335 protein)	anti-sigma cross-reacting protein homolog I alpha precursor	KNP-1a	GT335	nimilar to D and Orbany A 14 1 mg	SILLING IN E. COLL DUKF 2/A AND TO ZEOTATISH EN	Summa to E. Con Serr 2/1A and to zeotansn ES1 ES1 (zebrafish) protein, human homolog of	ES1 (zebrafish) protein, human homolog of ES1 (zebrafish) protein, human homolog of	ES1 (zebrafish) protein, human homolog of ES1 (zebrafish) protein, human homolog of ES1 (zebrafish) protein, human homolog of HES1
100001	10///1	12050.1	AAH15005.1 acti	:	•		NP 001092.1 bet	,	ATHUB acti	25099.1	1		AAH02409.1 acti	AAH04251.1 acti	AAH09275.1 acti	AAH13380.1 acti	AAH14861.1 acti	AAH16045 acti	45026.1	NP_004640.1 chr	Zeo	D20047			BAA12984.1 KN						
AAH						· N					2										F:(R-D)	7									
	, ,															7.			·	Mm.28984 U:(C-IR)				,		,					
		2			and the second second										,	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	: .			AA510875 N	NP_613067.1										

			DA A 21129 1	VAD I alaha sanatain		
			177170.1	ANY -1 aipua protein	74	243 9E-65
NM_009349	Mm.299	F:(C-R)	AAD04723.1	thioether S-methyltransferase-like; similar to P40936 (PID;g731019)	27.	271 9E-73
NP_033375.1		-2.05 U:(IR-D) 3.02				
}- '- '- '- '- '- '- '- '- '- '- '- '- '-			092020	INMT_HUMAN Indolethylamine N-methyltransferase (Aromatic alkylamine N-methyltransferase) (Indolamine N-methyltransferase)	267	2E-71
	,	:		(Amine N-methyltransferase)		
			AAF18304.1	AF128846 1 indolethylamine N-methyltransferase	792	2E-71
			F18306.1	AF128848 1 indolethylamine N-methyltransferase	267	2E-71
•	9		006765.3	indolethylamine N-methyltransferase; thioester S-methyltransferase-like	796	266 5E-71
i.	m arms 1,1		F18305.1	AF128847 1 indolethylamine N-methyltransferase	266	266 5E-71
			AAH33813.	Unknown (protein for IMAGE:5209218)	792	266 5E-71
			60.1	nicotinamide N-methyltransferase	235	239 6E-63
,			P40261	NNMT_HUMAN Nicotinamide N-methyltransferase	235	239 6E-63
		·		nicotinamide N-methyltransferase (EC 2.1.1.1)	. 239	239 6E-63
		:		nicotinamide N-methyltransferase	235	239 6E-63
			58.1	nicotinamide N-methyltransferase	235	239 6E-63
		- 1	AAH00234.1	AAH00234 nicotinamide N-methyltransferase	235	239 6E-63
NM_019813 NP_062787.1	Mm.19016 F:(C-IR)		,	DREB_HUMAN Drebrin (Developmentally regulated brain protein)	0 09/	0
1.10/200_11		V:(IR-D)				
		2.42				• •
			1	drebrin E (clone gDbh13)	760	0
		À.		drebrin B2	0 092	0
			BAA04480.1	drebrin E	760 0	. 0
	; ::		AAH00283.1	AAH00283 drebrin 1	760 0	0
	· ·		AAH07281.1	AAH07281 drebrin 1	760	0
			AAH07567.1	AAH07567 drebrin 1	760	0
			NP 004386.2	drebrin 1 isoform a; drebrin E; drebrin-1; drebrin E2	759 0	0
	: 1			hypothetical protein DKFZp434D064.1	704 0	0
L.	÷	•	353683.1	hypothetical protein	704 0	0
			NP 543157.1	drebrin 1 isoform b; drebrin E; drebrin-1; drebrin E2	703	0

1749 0		1749 0	1749 0	1749 0	741 0	630 e-180		628 e-179	628 e-179	628 e-179	628 e-179	623 e-178	623 e-178	499 e-140	499 e-140	498 e-140	498 e-140
_003026.1 TAL1 (SCL) interrupting locus; SCL interrupting locus		SIL protein	TIS	SIL protein	dJ18D14.1 (TAL1 (SCL) interrupting locus)	S-adenosylmethionine decarboxylase 1		S-adenosylmethionine decarboxylase 1 precursor	DCAM_HUMAN S-adenosylmethionine decarboxylase proenzyme (AdoMetDC) (SamDC) [Contains: S-adenosylmethionine decarboxylase alpha chain; S-adenosylmethionine decarboxylase beta chain]	adenosylmethionine decarboxylase (BC 4.1.1.50) precursor	S-adenosylmethionine decarboxylase proenzyme (EC 4.1.1.50) old gene name 'AMD'	B Chain B, Structure Of A Human S-Adenosylmethionine Decarboxylase Self-Processing Ester Intermediate And Mechanism Of Putrescine Stimulation Of Processing As Revealed By The H243a Mutant	A Chain A, Structure Of A Human S-Adenosylmethionine Decarboxylase Self- Processing Ester Intermediate And Mechanism Of Putrescine Stimulation Of Processing As Revealed By The H243a Mutant	A Chain A, Human S-Adenosylmethionine Decarboxylase	C Chain C, Human S-Adenosylmethionine Decarboxylase	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With Methylglyoxal Bis- (Guanylhydrazone)	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound 5'-Deoxy-5'-[n- Methyl-N-(2-Aminooxyethyl) Amino]adenosine
NP_003026.1		A41685	AAA60550.1	AAK51418.1	CAB72102.1	AAH00171.1		NP 001625.1	P17707	DCHUDM	AAA51716.1	1JL0	1JL0	1JEŅ	1JEN	1I7C	1172
F:(C-IR)	U:(IR-D) 2.51					F:(C-IR)	-2.6 U:(IR-D) 3.96									,	
Mm.3988						Mm.7880										,	
NM_009185 Mm.3988	NP_033211.1					NM_009665	NP_033795.1										

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498 e-140	8 e-140	4 e-133	474 e-133	201 2E-51		1 2E-51	1 2E-51	0 0			000	000	5 0	50.	2 1E-99	301 2E-81	1 2E-81		1 2E-81	301 2E-81	296 5E-80
46	498	474	47,	70		201	201	089			089	089	9/9	9/9	362	30	301		301	8	73
A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound 5'-Deoxy-5'-[(3-Hydrazinopropyl)methylamino]adenosine	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound S-Adenosylmethionine Methyl Ester	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently One-2'-Amidinohydrazone	C Chain C, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With 4-Amidinoindan-1-One-2'-Amidinohydrazone	KIAA1749 protein		hypothetical protein FLJ14957	unnamed protein product	wingless-type MMTV integration site family, member 11 precursor			WN11_HUMAN WNT-11 protein precursor	WNT11	WNT11	HWNT1	unnamed protein product	WNT4	wingless-type MMTV integration site family, member 4 precursor; signaling protein	WINI-+, WINI-+ ploted precusor		AF316545 1 signaling protein WNT-4	WNT4 precursor
1179	1I7B	117M	117M	BAB21840.1		NP 116255.1	BAB55415.1	NP_004617.2			096014	BAB72099.1	CAA73223.1	CAA74159.1	BAC11683.1	BAC23080.1	NP_110388.2	DECTOR	F30/U3	AAK.>1699.1	AAG38658.1
	3	: 	, , , , , , , , , , , , , , , , , , ,	F:(C-IR) -2.43	U:(JK-LJ) 2.5		:	 F:(C-IR)	-2.4 U:(C-D) 2.09	U:(IR-D) 2.84								1			
				Mm.87428			. "	Mm.22182 F:(C-IR)													
				NM_026599 NP_080875.1				NM_009519	NP_033545.1						,						

62	69	- 69	69	69	69	69	69	69	69	<u>1</u>				·	,	-									
295 IE-79	262 1E-69	262 1E-69	262 1E-69	262 1E-69	262 1E-69	261 3E-69	261 3E-69	261 3E-69	261 3E-69	255 1E-67	1030 0		_	1030 0	1030 0	·	1030 0	1030 0	1030 0	1030 0	1030 0	1028 0	1028 0	1005 0	0 669
25			. 2(2(2(2(2(2(2(2.	10.	:	_	10			12	12	12	2	=	=		10	H
14122446 2 (similar to Mouse Wut-4 protein)	T	 	WN5B HUMAN WNT-5B protein precursor	T	1		WN5A HUMAN WNT-5A protein precursor	proto-oncogene Wnt-5A precursor		WNT5b precursor	1 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3			similar to 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (6PF-2-K/Fru-2,6-P2ASE brain/placenta-type isozyme) (iPFK-2)	F263_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (6PF-2-	K/Fin-z,o-rzzase oram piacenta-type isozymej (r r.k-z) [incauces, o-prospaci moso- 2-kinase; Fructose-2,6-bisphosphatase]	6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase	Т.	1	1 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	T	1	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46)	+-	
CAB52601 1	NP_116031.1	NP_110402.2	O9H1J7	AAH01749.1	BAB62039.1	NP_003383.1	P41221	A489,14	AAA16842.1	AAG38659.1	NP_004557.1	;	•.	XP_096349.2	Q16875		BAA08624.1	AAD08818.1	AAL40083.1	AAH40482.1	2208342A	AAB99795.1	JC4626	A A C 62000 1	CAA06605.1
											F:(C-IR)	-2.39 11:(TR-D)	2.05										~		
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0 694	0 889	0 889	0 089	080	0/0/9	0 0/9		0 0/9	0 0/9	0 0/9	0 699	910 0				910 0	3 0	609 e-173	609 e-173	609 e-173	609 e-173	609 e-173	609 e-173
69	89	89	89	89	<i>L</i> 9	<i>L9</i>		<i>L</i> 9	<i>L</i> 9	<i>L9</i>	99	91	• .			91	773	09	8	g	9.	9	9
F262_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2 (6PF-2-KFru-2,6-P2ASE heart-type isozyme) (PFK-2/FBPase-2) [Includes: 6-phosphofructo-2-kinase; Fructose-2,6-bisphosphatase]	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2; Fructose-2,6-bisphosphatase, cardiac isozyme	6-phosphofructo-2-kinase	6-phosphofructo-2-kinase heart isoform	AF470623_1 PFK2/F26DPase	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	F264_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (6PF-2- F/Rm-2,6-D2ASH testis-type isozyme) (Includes: 6-phosphofructo-2-frage)	Fructose-2,6-bisphosphatase]	6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase	testis 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase	AAH10269 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46	cyclic nucleotide gated channel beta 3; cyclic nucleotide-gated chanel, beta 3				AF272900_1 cone photoreceptor cyclic nucleotide-gated channel beta subunit	AF228520 1 cone photoreceptor cGMP-gated cation channel beta-subunit	CNG4_HUMAN Cyclic-nucleotide-gated cation channel 4 (CNG channel 4) (CNG-4) (CNG4) (Cyclic nucleotide-gated cation channel modulatory subunit)	cyclic nucleotide-gated cation channel	cGMP-gated cation channel 2, rod	cGMP-gated cation channel subunit 2, cGMP-gated cation channel, subunit beta, hRCNC2 [human, retinal rod cells, Peptide, 909 aa]	cyclic nucleotide-gated cation channel	cGMP-gated cation channel beta subunit
060825	NP_006203.1	CAA06606.1	BAB19681.1	AAL99386.1	NP 004558.1	Q16877	· .	BAA18921.1	AAD09427.1	AAH10269.1	JC5871	NP_061971.2				AAF86274.1	AAF80179.1	Q14028	AAA65620.1	S32538	AAB32607.1	1912307A	AAB63387.1
												F:(C-IR)	-2.33	3.63	U:(IR-D) 2.84				,				
	3 2 3										1	Mm.10357	5					:					
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			1000100	and is any lacked a correct hate 1. wells mislestide asted channel	609	609 le-173
		,		cyclic interceptor, cGMP gated 3 (gamma)-like		
			AAC04830.1	rod photoreceptor CNG-channel beta subunit	609	e-173
			65619.1	cyclic nucleotide-gated cation channel	. 598	e-170
				cyclic nucleotide-gated channel protein	269	269 3E-71
			289.1	cyclic nucleotide gated channel alpha 3	269	269 3E-71
			1	CNG3 HUMAN Cyclic-nucleotide-gated cation channel alpha 3 (CNG channel alpha	569	269 3E-71
				3) (CNG-3) (CNG3) (Cyclic nucleotide gated channel alpha 3) Cone photoreceptor	-	
			,	cciMP-gated channel alpha subunit)		
			317440.1	cone photoreceptor cGMP-gated channel alpha subunit	269	3E-71
			NP 000078.1	cyclic nucleotide gated channel alpha 1	268	268 6E-71
			161	cGMP-gated cation channel, rod photoreceptor	268	268 6E-71
			10.1	cGMP-gated cation channel protein	268	268 6E-71
1	Mm.78718 F:(C-IR		NP_057305.1	dynactin 4 (p62); dynactin p62 subunit	0 988	0
NF_080378.1		7-2.21 [1:(TR-D)				
		2.61				
			XP 041993.1	similar to dynactin 4 (p62); dynactin p62 subunit	886	0
			AAF03896.1	AF195120 1 dynactin p62 subunit	988	0
			BAA91066.1	umamed protein product	0 988	0
	,			dynactin 4 (p62)	883 0	0
-			T47143	hypothetical protein DKFZp761J032.1	282	282 8E-76
			CAB82417.1	hypothetical protein	282	282 8E-76
-	,	-	-			
NM_007755 NP_031781.1	Mm.22062 F:(C-IR) -2.2 U:(IR-D	F:(C-IR) -2.2 U:(IR-D)	NP_085097.2	cytoplasmic polyadenylation element binding protein; hypothetical protein FLJ13203 similar to cytoplasmic polyadenylation element binding protein; cytoplasmic polyadenylation element-binding protein	1039	0
		2.11				
			AAK01239.1	AF329402_1 cytoplasmic polyadenylation element-binding protein long form	. 1039	0
			AAK01240.1	AF329403_1 cytoplasmic polyadenylation element-binding protein short form	868	0
,			AAH35348.1	Similar to cytoplasmic polyadenylation element binding protein	088	0
			BAB14496.1	unnamed protein product	878 0	. 0
			NP 055727.1	KIAA0940 protein	207	207 SE-53

				KIA A 0940 profein	207 15	5B-53
			XP 047672.4	similar to RIKEN cDNA 4930447D24	207 6E-53	E-53
			BAB21764.1	KIAA1673 protein	207 6E-53	E-53
	·			Unknown (protein for MGC:46609)	207 GE-53	E-53
				Similar to KIAA0940 protein	203	203 9E-52
NM_008422	Mm.39092	F:(C-IR)	04968.2	Shaw-related voltage-gated potassium channel protein 3; Kv3.3; voltage-gated	778 0	
NP 032448.1		-2.17 U:(C-D)		potassium channel protein KV3.3		
		2.07				
1		U:(IR-D) 2.33			٠.	
			Q14003	KNC3_HUMAN Potassium voltage-gated channel subfamily C member 3 (Potassium channel Kv3.3) (KSHIIID)	0 8//	
		4	AAC24118.1	Shaw type potassium channel Kv3.3	778 (0
	- ,		NP_004967.1	Shaw-related voltage-gated potassium channel protein 1; voltage-gated potassium channel protein KV3.1; potassium voltage-gated channel subfamily C member 1	612	612 e-175
	ı		P48547	KNC1_HUMAN Potassium voltage-gated channel subfamily C member 1 (Potassium channel Kv3.1) (Kv4) (NGK2)	612	e-175
			A46020	potassium channel KCNC1	612	e-175
			AAB25764.1	voltage-gated potassium channel; NGK2	612	612 e-175
	,		NP_004969.2	Shaw-related voltage-gated potassium channel protein 4 isoform a; voltage-gated potassium channel protein KV3.4	571	e-162
	ŧ		CAC19684.1	dI1003J2.3.2 (potassium voltage-gated channel, Shaw-related subfamily, member 4)	571	e-162
		,	Q03721	CIKG HUMAN Potassium voltage-gated channel subfamily C member 4 (Potassium channel Kv3.4) (KSHIIIC)	571	571 e-162
			AAA57263.1	potassium channel protein	.571	e-162
			NP_720198.1	Shaw-related voltage-gated potassium channel protein 4 isoform b; voltage-gated potassium channel protein KV3.4	571	e-1 <u>6</u> 2
			CAC19683.1	dJ1003J2.3.1 (potassium voltage-gated channel, Shaw-related subfamily, member 4)	571	e-162
			NP 715624.1	Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2c	955	e-158
			BAC04407.1	unnamed protein product	925	556 e-158
			NP 631875.1	Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2b	955	556 e-158
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			A A I 27272 1	AF96896 1 voltage gated notassium channel Kv3 2h	556	556 e-158
1			214.1	11 200000 I volumes gardy pounsituant channes are over	255	556 0 158
	42.		NP 6318741	Potassium voitage-gated potassium channel suoraumy Curemost z Shaw-related voltage-gated notassium channel protein 2 isoform KV3.2a	556	556 e-158
			273.1	AF268897 1 voltage gated potassium channel Kv3.2a	556	556 e-158
NM_011749 NP_035879.1	Mm.417	F:(C-IR) -2.05	Q9UQR1	Z148_HUMAN Zinc finger protein 148 (Zinc finger DNA binding protein 89) (Transcription factor ZBP-89)	1460 0	0
		U:(R-D) 2.34				
			AAC39926.1	zinc finger DNA binding protein 89 kDa	1460 0	0
			AAL99917.1	AF432210 1 CLL-associated antigen KW-10	1458	. 0
	1.0		NP_068799.1	zinc finger protein 148 (pHZ-52); zinc finger protein 148 (pHZ-52), BERF-1, ZBP-89	1455	. 0
			CAA15422.1	ZBP-89 protein	1455	0
			A54693	CACCC box-binding protein ht-beta	744 0	0
			AAA36664.1	CACCC box-binding protein	743 0	0
			AAH35\$91.1	Similar to zinc finger protein 148 (pHZ-52)	714 0	0
			AAB57692.1	zinc finger binding protein homolog	0 692 0	0
			CAB70967.1	zinc finger protein	371	e-102
			NP 036614.1	zinc finger protein 281; ZNP-99 transcription factor	371	e-102
			Q9Y2X9	Z281_HUMAN Zinc finger protein 281 (Zinc finger DNA binding protein 99) (Transcription factor ZBP-99) (GC-box-binding zinc finger protein 1)	371	371 e-102
			JC7089	zinc finger binding protein-99	371	e-102
			AAD21084.1	zinc finger DNA binding protein 99	371	e-102
			CAB70968.1	zinc finger protein	371	e-102
NM_030566 NP_085043.1	Mm.35467	7 F:(C-IR) -2.05 U:(C-D) 2.62 U:(R-D) 2.11	NP_079092.1	Fos-related antigen	621	e-177
			BAB15594.1	unnamed protein product	621	e-177
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		699	663	663 0	657	635 0	635 10	474	474	474	474	474	474	474	474	474	474	133	431	428
		LIPG_HUMAN Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	triacylglycerol lipase (EC 3.1.1.3) precursor, gastric	gastric lipase precursor	gastric lipase precursor	A Chain A, Crystal Structure Of Human Gastric Lipase	B Chain B, Crystal Structure Of Human Gastric Lipase	lysosomal acid lipase	lysosomal acid lipase	lysosomal acid lipase	AAH12287 Similar to lipase A, Iysosomal acid, cholesterol esterase (Wolman disease)	lysosomal acid lipase (EC 3.1.1) / sterol esterase (EC 3.1.1.13) precursor	lysosomal acid lipase; sterol esterase	lysosomal acid lipase/cholesteryl ester hydrolase	lipase A precursor; Lipase A, lysosomal acid, cholesterol esterase	LICH_HUMAN Lysosomal acid lipase/cholesteryl ester hydrolase precursor (LAL) (Acid cholesteryl ester hydrolase) (Sterol esterase) (Lipase A) (Cholesteryl esterase)	lysosomal acid lipase/cholesteryl esterase		similar to Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	
		P07098.	S07145	CAA29413.1	CAA29414.1	1HLG	1HLG	G01416	AAB60328.1	CAA83495.1	AAH12287.1	S41408	CAA54026.1	AAB60327.1	NP 000226.1	P38571	AAA59519.1	XP 089555.2	XP 061222.1	CAC78754.1
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The appended claims are to be treated as a non-limiting recitation of preferred embodiments.

In addition to those set forth elsewhere, the following references are hereby incorporated by reference, in their most recent editions as of the time of filing of this application: Kay, Phage Display of Peptides and Proteins: A Laboratory Manual; the John Wiley and Sons Current Protocols series, including Ausubel, Current Protocols in Molecular Biology; Coligan, Current Protocols in Protein Science; Coligan, Current Protocols in Immunology; Current Protocols in Human Genetics; Current Protocols in Cytometry; Current Protocols in Pharmacology; Current Protocols in Neuroscience; Current Protocols in Cell Biology; Current Protocols in Toxicology; Current Protocols in Field Analytical Chemistry; Current Protocols in Nucleic Acid Chemistry; and Current Protocols in Human Genetics; and the following Cold Spring Harbor Laboratory publications: Sambrook, Molecular Cloning: A Laboratory Manual; Harlow, Antibodies: A Laboratory Manual; Manipulating the Mouse Embryo: A Laboratory Manual; Methods in Yeast Genetics: A Cold Spring Harbor Laboratory Course Manual; Drosophila Protocols; Imaging Neurons: A Laboratory Manual; Development of Xenopus laevis: A Laboratory Manual; Antibodies: A Laboratory Manual; At the Bench: A Laboratory Navigator; Cells: A Laboratory Manual; Methods in Yeast Genetics: A Laboratory Course Manual; Discovering Neurons: The Experimental Basis of Neuroscience; Genome Analysis: A Laboratory Manual Series ; Laboratory DNA Science; Strategies for Protein Purification and Characterization: A Laboratory Course Manual; Genetic Analysis of Pathogenic

Bacteria: A Laboratory Manual; PCR Primer: A Laboratory
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Reference to known method steps, conventional methods steps, known methods or conventional methods is not in any way an admission that any aspect, description or embodiment of the present invention is disclosed, taught or suggested in the relevant art.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying knowledge within the skill of the art (including the contents of the references cited herein), readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present invention. Therefore, such adaptations and modifications are intended to be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the present specification is to be interpreted by the skilled artisan in light of the

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teachings and guidance presented herein, in combination with the knowledge of one of ordinary skill in the art.

Any description of a class or range as being useful or preferred in the practice of the invention shall be deemed a description of any subclass (e.g., a disclosed class with one or more disclosed members omitted) or subrange contained therein, as well as a separate description of each individual member or value in said class or range.

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The description of preferred embodiments individually shall be deemed a description of any possible combination of such preferred embodiments, except for combinations which are impossible (e.g, mutually exclusive choices for an element of the invention) or which are expressly excluded by this specification.

If an embodiment of this invention is disclosed in the prior art, the description of the invention shall be deemed to include the invention as herein disclosed with such embodiment excised.